W. Theilheimer

Synthetic Methods of Organic Chemistry

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Synthetic method..

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W. Theilheimer

Synthetic Methods of Organic Chemistry

An Annual Survey

Synthetische Methoden der Organischen Chemie

Jahresbericht

Vol. 6

Mit deutschem Register-Schlüssel

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From the Prefaces to the Preceding Volumes

New methods for the synthesis of organic compounds, improvements of known methods, and also old proved methods scattered in periodicals, are being recorded continuously in this book series.

An attempt has been made to develop the system of Weygand (Organic Preparations, Interscience Publishers, Inc., New York, 1945), and to group the reactions on a simple, although purely formal, basis. This has led to the invention of reaction symbols that can be classified systematically so that the methods can be treated without knowledge of the current trivial and author names (e.g., "Oxidation" and "Friedel-Crafts reaction").

Readers accustomed to the common notations will find these in the subject index. In many cases, particularly in searching for complex reactions, use of the classification system may be avoided by consulting the subject index. It is thought that the volumes should be used for immediate reference in the laboratory. They should provide a quick survey of the situation at hand, and obviate the necessity of first searching the entire literature. Syntheses are therefore recorded in the subject index by starting materials and end products, along with the systematic arrangement for the methods. This makes possible a subclassification within the reaction symbols by reagents, a further methodical criterion. Starting with Volume 5, a table indicating the sequence of the reagents has been included. It may help the reader to locate reactions in the body of the text, particularly within large chapters. This table also contains such frequently used reagents as NaOH and HCl, which are not included in the subject index. Another innovation is the indexing of complex compounds with cross references under the related simpler compounds. General terms, such as synthesis, replacement, heterocyclic compounds, may also be brought to the special attention of the reader.

The abstracts are limited to the information needed for an appraisal of the applicability of a desired synthesis. This includes the number and nature of the reaction steps, the yield, and the important literature in question. In order to carry out a particular synthesis it is therefore still necessary to have recourse to the original papers or, at least, to an abstracting journal. In order to avoid repetition, selections are made on the basis of most detailed description and best yields, whenever the same method is used in similar cases. Continuations of papers already included will not be abstracted, unless they contain essentially new information. They may, however, be quoted at the place corresponding to the abstracted papers. These brief literature references were newly introduced in the 3rd volume.

Furthermore, to avoid a "jungle" of references, the following limitations have been decided on: Papers are not included, if their content does not fit the subject matter of "Synthetic Methods" and if they can be found easily in the indices of the abstract journals. Less accessible and readable papers, such as the Russian ones, are only abstracted, as a rule, if the method in question is described nowhere else.

Syntheses that are split into their various steps, which are recorded in different places, can be followed with the help of the notations *startg. m. f.* (starting material for the preparation of ...) and *prepn. s.* (preparation, see).

Aus den Vorworten zu den vorhergehenden Bänden

In dieser Buchreihe sollen neue Methoden zur Synthese organischer Verbindungen, Verbesserungen bekannter und auch bewährte ältere Methoden, die sich in den in Fachzeitschriften veröffentlichten Originalarbeiten verstreut vorfinden, laufend registriert werden.

Aufbauend auf der Weygandschen Systematik wurde versucht, alle Reaktionen an Hand weniger einfacher, wenn auch rein formaler Richtlinien zu ordnen. Dies führte zur Ausarbeitung von Reaktions-Formelzeichen, die sich im Gegensatz zu den bisherigen Trivial- bzw. Autorennamen, wie Oxydation, Friedel-Crafts-Synthese, systematisch anordnen lassen. Man kann so die Methoden, ohne ihren Namen zu kennen, mittels des Formelzeichens auffinden.

Benutzer, die an die alten Bezeichnungen gewöhnt sind, finden diese im alphabetischen Register, das in vielen Fällen den Gebrauch der Systematik entbehrlich machen und besonders zum Aufsuchen komplizierter Reaktionen mit Vorteil benutzt werden dürfte. Da die Sammlung für die Handbibliothek am Arbeitsplatz im Laboratorium gedacht ist, soll sie eine rasche Orientierung gestatten, ohne daß fürs erste die Literatur der Instituts- oder Werkbibliothek herangezogen werden muß. Neben der systematischen Registrierung der Methoden werden deshalb im alphabetischen Register auch Synthesen durch ihre Ausgangs- und Endprodukte registriert. Dies ermöglicht es, im Text, innerhalb der Reaktionszeichen, nach einem weiteren methodischen Kriterium, nämlich den Hilfsstoffen einzuteilen. Beginnend mit Band 5 ist eine Tafel aufgenommen worden, die die Reihenfolge der Hilfsstoffe angibt. Sie

dürfte zum Aufsuchen von Reaktionen im Text, besonders in großen Kapiteln, nützlich sein. Sie enthält auch so häufig gebrauchte Hilfsstoffe wie NaOH und HCl, die im alphabetischen Register nicht aufgeführt sind. Neuartig ist ferner die Registrierung der komplizierten Verbindungen. Auf Sammelbegriffe wie Aufbau, Austausch, Heterocyclen sei noch besonders hingewiesen.

Die Referate beschränken sich auf das zur Beurteilung der Zweckmäßigkeit einer Synthese Notwendige, wie Zahl und Art der Reaktionsstufen, die Ausbeute, wichtige, die Methode betreffende Literatur usw. Vor Ausführung einer bestimmten Synthese ist es deshalb erforderlich, das Chemische Zentralblatt oder ein anderes Referatenblatt und, wenn möglich, auch die Originalarbeit zu Rate zu ziehen. Zur Vermeidung von Wiederholungen wurden bei der Anwendung einer Methode in ähnlichen Fällen diejenigen ausgewählt, die am ausführlichsten beschrieben sind und die besten Ausbeuten geben. Fortsetzungen bereits aufgenommener Arbeiten, die nichts wesentlich Neues bringen, werden nicht mehr referiert, evtl. aber an der Stelle der aufgenommenen Arbeit zitiert. Diese kurzen Literaturzitate wurden im 3. Band neu eingeführt.

Um ferner das Material nicht zu sehr auf Kosten der Uebersicht anschwellen zu lassen, werden Veröffentlichungen, die nicht ganz in den Rahmen der «Synth. Meth.» passen und die in den Sachregistern der Referatenblätter leicht aufgefunden werden können, nicht aufgenommen. Arbeiten aus schwerer zugänglichen und lesbaren Zeitschriften, wie z. B. den russischen, werden im allgemeinen nur dann referiert, wenn die betreffende Methode sonst nirgends beschrieben ist.

Synthesen, die in ihre Stufen zerlegt und an verschiedenen Stellen eingeordnet sind, können mit Hilfe der Vermerke *startg. m. f.* (Ausgangsmaterial für die Darstellung von . . .) und *prepn. s.* (Darstellung siehe) zusammengesetzt werden

Preface to Volume 6

Volume 6 continues the collection of organic synthetic methods over the period of one year. It consists of abstracts from papers published mostly in 1949 and 1950, with supplementary references from 1951.

This volume is meant to be the first one of a second series. New references to material in the preceding volumes have, however, been included in the text. The index also contains a few additional or revised entries to former volumes.

Since publications dealing with organic chemistry are increasing from year to year, some omissions may have occurred. The author will,

therefore, be grateful if important methods not yet included are brought to his attention.

Grants from the chemical industry once again made possible the continuation of this book series. They are acknowledged on a separate page. Thanks are due again to Dr. J. A. Aeschlimann, Director of Chemical Research, Hoffmann-La Roche, Inc., for liberally providing me with library and office facilities, and to Professor H. Erlenmeyer, Basle, Switzerland, for his continued interest in this enterprise. Finally, I want to thank Dr. John T. Plati for having read the text and giving me valuable advice, and again to Dr. and Mrs. Sorkin-Brügger, Basle, Switzerland, for their thorough proof-reading.

Nutley (New Jersey/USA), June 1952. W. Th.

Vorwort zu Band 6

Der vorliegende 6. Band setzt die Sammlung organisch-synthetischer Methoden über den Zeitraum eines Jahres fort. Er enthält hauptsächlich Referate von Arbeiten aus den Jahren 1949 und 1950 mit Ergänzungen aus dem Jahre 1951.

Dieser Band ist als der erste einer zweiten Serie gedacht. Jedoch enthält der Text auch neue Zitate zu Referaten aus früheren Bänden. Im Register finden sich ebenfalls einige zusätzliche und revidierte Schlagworte zu diesen Bänden.

Da die Zahl der Veröffentlichungen auf dem Gebiete der organischen Chemie in den letzten Jahren sehr angewachsen ist, konnten Lücken nicht vermieden werden. Wir wären deshalb dankbar, wenn wir auf wichtige Methoden aufmerksam gemacht würden, die in unserer Sammlung noch nicht enthalten sind.

Nutley (New Jersey/USA), im Juni 1952. W. Th.

Method of Classification

The following directions serve to explain the system of Classification.

1. Reaction Symbols.

The first part of the symbol refers to the chemical bonds formed during the reaction. These bonds appear in the reaction symbols as the symbols for the two elements that have been linked together (e.g., the bond between hydrogen and nitrogen, as HN). The order of the elements is the same as in *Chemisches Zentralblatt* and in Beilstein's *Handbuch der organischen Chemie:* H, O, N, Hal (Halogen), S, and the remaining elements (Rem). C is always placed last.

The "principle of the latest position" determines the order of the element symbols, and is used whenever possible.

The methods of obtaining a particular chemical bond are subdivided according to methods of formation. Four types are distinguished: addition (⇓), rearrangement (⤵), exchange (⇅), and elimination (⇑). The next part of the symbol refers to the types of bond which are destroyed in the reaction. Of the elements which form these bonds, in general two appear in the reaction symbols of addition and rearrangement and one appears in the reaction symbols of exchange and elimination.

The use of the reaction symbols will be made clearer by the following simplifying stipulations. (*1*) The chemical bond is rigidly classified according to structural formula, with no consideration of the mechanism of the reaction. (*2*) Double or triple bonds are treated as being equivalent to two or three single bonds, respectively. (*3*) Generally speaking, only stable organic compounds are taken into consideration. Intermediary compounds, such as Grignard compounds and sodiomalonic esters, and anorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Examples:

see Volume II, page viii (Interscience Publishers)

Systematic Survey

see page 393.

2. Reagents.

A further subdivision, not expressed by the reaction symbols, is made on the basis of the reagents characteristic of the reaction. The order usually follows that of the periodic system. Reagents made up of several components are arranged according to the significant element for the reaction (e.g., $KMnO_4$ under Mn, $NaClO$ under Cl). When a constituent of the reagent goes into the products of the reaction, the remainder of the reagent, which acts as a carrier of this constituent, is the criterion for the classification; for example, phosphorus is the carrier in a chlorination with PCl_5 and sodium in a nitrosation with $NaNO_2$. A table indicating the sequence of the reagents may be found on page 395.

3. The material between the listings of the reagents is arranged with the simple examples first and the more complicated ones following.

4. When changes in more than one chemical bond occur during a reaction, as, for example, in the formation of a new ring, or if the reaction can be carried out in different ways, these reactions are introduced in several places when necessary. The main entry in such cases will usually follow according to the "principle of the latest position"; the other entries will be cross-referenced back to it.

Systematik

Für die Reihenfolge der Methoden gelten folgende Richtlinien:

1. Reaktionszeichen.

Die Einteilung erfolgt zuerst nach den Bindungen, die bei einer Reaktion entstehen. Diese erscheinen im Reaktions-Formelzeichen in Gestalt ihrer beiden Elementsymbole, z. B. die Bindung zwischen Wasserstoff und Stickstoff als HN. Die Reihenfolge der Elemente ist die gleiche wie im Chemischen Zentralblatt und in Beilsteins Handbuch der organischen Chemie: H, O, N, Hal (Halogen), S, Rem (Uebrige Elemente), C steht an letzter Stelle.

Das «*Prinzip der letzten Stelle*» bestimmt die Reihenfolge der Elementsymbole und ist auch sonst nach Möglichkeit immer angewandt worden.

Die Methoden zur Herstellung einer bestimmten Bindung werden nach ihrer Bildungsweise eingeteilt. Es werden 4 Fälle unterschieden: Aufnahme (⇓), Umlagerung (↷), Austausch (⇅) und Abgabe (⇑).

Die weitere Einteilung ergibt sich aus den Bindungen, die bei der Reaktion gelöst werden. Von den Elementen, die an diesen Bindungen beteiligt sind, werden im allgemeinen bei Aufnahme und Umlagerung zwei, bei Austausch und Abgabe eines in das Reaktionszeichen aufgenommen.

Die Bildung des Reaktionszeichens wird durch folgende vereinfachende Annahmen erleichtert:

1. Die Bindungen für die Registrierung ergeben sich rein formal aus den Strukturformeln, ohne daß auf Reaktionsmechanismen Rücksicht genommen wird.
2. Doppel- und Dreifachbindungen werden 2 bzw. 3 Einfachbindungen gleichgesetzt.
3. Es werden in der Regel nur stabile organische Verbindungen berücksichtigt, Zwischenprodukte, wie z. B. Grignard-Verbindungen, Na-Malonester und anorganische Reaktionspartner, wie z. B. Salpetersäure, werden deshalb nicht zur Bildung des Reaktionszeichens herangezogen.

Beispiele

siehe Band 2, Seite VI

Systematische Uebersicht

siehe Seite 393

2. Hilfsstoffe.

Eine weitere Unterteilung, die im Reaktionszeichen nicht mehr zum Ausdruck kommt, wird nach den für die Reaktion charakteristischen Hilfsstoffen vorgenommen. Ihre Reihenfolge richtet sich im wesentlichen nach dem periodischen System. Hilfsstoffe, die sich aus mehreren Bestandteilen zusammensetzen, werden nach demjenigen eingeteilt, der für die Reaktion verantwortlich ist, z. B. steht $KMnO_4$ bei Mn, NaClO bei Cl. Geht ein Bestandteil des Hilfsstoffs in das Reaktionsprodukt ein, dann ist der Rest als Träger dieses Bestandteils für die Einordnung maßgebend; das ist z. B. bei einer Chlorierung mit PCl_5 Phosphor, bei einer Nitrosierung mit $NaNO_2$ Natrium. Eine Tafel der in diesem Band verwendeten Reihenfolge der Hilfsstoffe befindet sich auf Seite 395.

3. Innerhalb dieser Unterteilung sind die einzelnen Referate von einfachen zu komplizierten Beispielen fortschreitend angeordnet.

4. Treten bei einer Reaktion Veränderungen an mehreren Bindungen ein, wie z. B. bei Ringschlüssen, oder kann sie auf verschiedene Art durchgeführt werden, dann wird sie, falls notwendig, an mehreren Stellen eingeordnet. Das Hauptzitat steht in diesen Fällen in der Regel an der letzten Stelle; an den übrigen Stellen befinden sich Hinweise auf dieses.

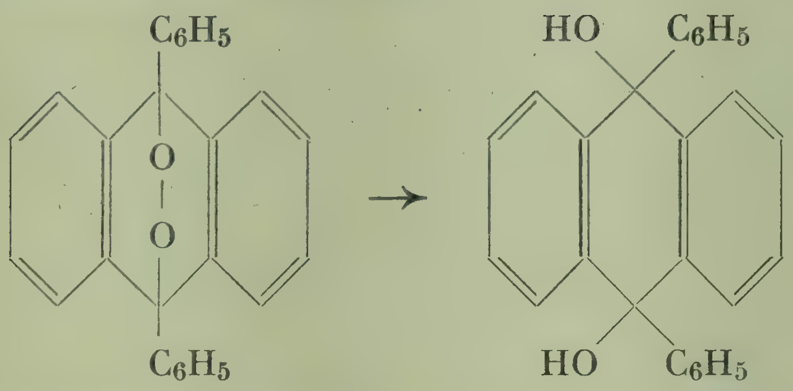
Formation of H—O Bond

Uptake

Addition to Oxygen **HO ⇓ O**

Phenyl magnesium bromide *C_6H_5MgBr*

Hydroxy compounds from peroxides ←

1. 

9,10-Diphenylanthracene peroxide and benzene added to an ethereal soln. of phenyl-MgBr, refluxed 2 hrs., and kept overnight at room temp. → 9,10-dihydroxy-9,10-diphenyldihydroanthracene. Y: 85%. F. e. s. A. Mustafa, Soc. *1949,* 1662.

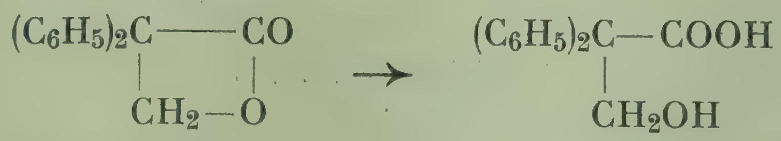
Addition to Oxygen and Carbon **HO ⇓ OC**

Potassium hydroxide/alcohol *KOH*

γ-Pyrone ring opening C
s. *6,* 128

Sulfuric acid/acetic acid *H_2SO_4/CH_3COOH*

Hydroxycarboxylic acids from lactones ←

2. 

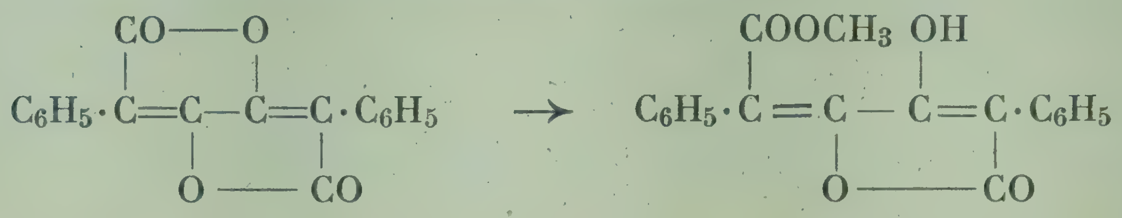
$$\begin{array}{l}(C_6H_5)_2C\text{——}CO \\ \quad\quad\quad | \quad\quad\quad | \\ \quad\quad CH_2-O\end{array} \rightarrow \begin{array}{l}(C_6H_5)_2C-COOH \\ \quad\quad\quad | \\ \quad\quad CH_2OH\end{array}$$

A soln. of α,α-diphenyl-β-propiolactone in H_2SO_4-acetic acid-water heated 7 hrs. on a steam bath → α-phenyltropic acid. Y: 83%. H. E. Zaugg, Am. Soc. *72,* 3001 (1950).

Hydrochloric acid *HCl*

Hydroxycarbalkoxylactones from dilactones ←

3.



A suspension of pulvinic acid lactone in methanol and some concd. HCl refluxed 15 min. → vulpinic acid. Y: 90%. F. e. s. R. L. Frank, G. R. Clark, and J. N. Coker, Am. Soc. *72,* 1824 (1950).

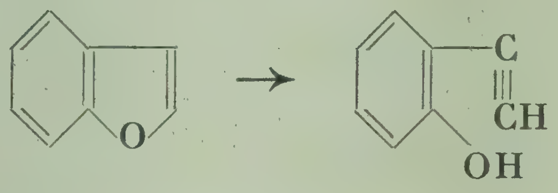
Rearrangement

Hydrogen/Carbon Type HO ↶ HC

Sodium/pyridine *Na/C_5H_5N*

Acetylene derivatives from benzofurans ↻

4.

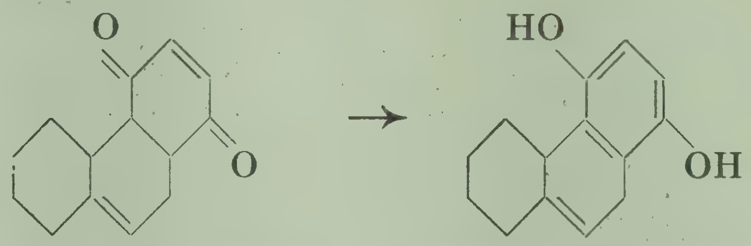


Coumarone refluxed 4 hrs. with Na in pyridine at an oil bath temp. of 180-190° → o-hydroxyphenylacetylene. Y: 84%. V. Prey and G. Pieh, M. *80,* 790 (1949).

Stannous chloride *$SnCl_2$*

Quinols from endiones ←

5.



$SnCl_2$ and HCl added to a soln. of 1,4-diketodecahydrophenanthrene in ethanol under N_2, and refluxed 1 hr. on a water bath → 1,4-dihydroxy-4b,5,6,7,8,10-hexahydrophenanthrene. Y: 96%. C. A. Grob, W. Jundt, and H. Wicki, Helv. *32,* 2427 (1949).

Exchange

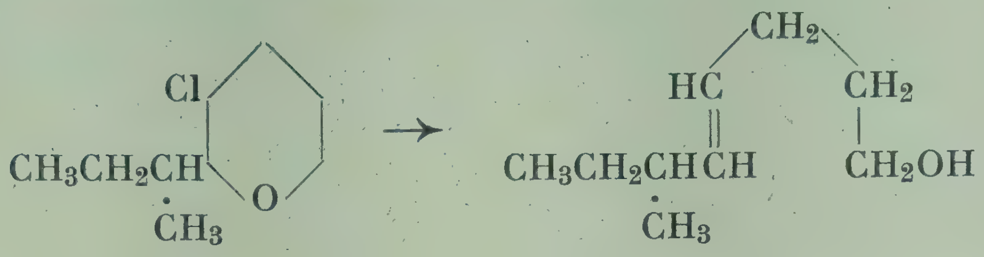
Halogen ↾ HO ⇅ Hal

Sodium *Na*

Ethylenealcohols from cyclic halogenoethers ↻

Synthesis with addition of 4 and 5 C-atoms

6.



Crude mixed (±)*cis-trans*-2-*sec*-butyl-3-chlorotetrahydropyran added dropwise to a stirred suspension of powdered Na in dry ether and allowed to stand overnight → (±)-*trans*-6-methyl-4-octen-1-ol. Y: 85%.—By using tetrahydrofuran derivatives as intermediates, a chain extension by 4 C-atoms can be achieved. F. e. s. L. Crombie and S. H. Harper, Soc. *1950*, 2685, 1707, 1714; s. a. R. C. Brandon, J. M. Derfer, and C. E. Boord, Am. Soc. *72*, 2120 (1950).

Sodium sulfide *Na_2S*

Sulfinic acids from sulfonic acid chlorides $SO_2Cl \rightarrow SO_2H$

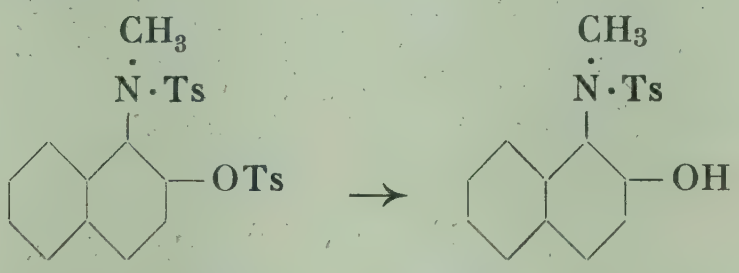
7. $Na_2S \cdot 9H_2O$ gradually added with stirring below 40° to a suspension of 1,5-anthraquinonedisulfonyl chloride (from the di-K salt and PCl_5), and stirring continued for 30 min. → 1,5-anthraquinonedisulfinic acid. Y: 83.5% based on disulfonic acid. F. e. s. V. V. Kozlov and D. D. Smolin, Ж *19*, 740 (1949); C. A. *44*, 3479a.

Sulfur ↑ HO ⇅ S

Potassium hydroxide *KOH*

Selective detosylation OTs → OH

8.



1-p-Toluenesulfonmethylamido-2-naphthyl p-toluenesulfonate (prepn. s. 410) refluxed 2 hrs. in alc. KOH → 1-p-toluenesulfonmethylamido-2-naphthol. Y: 94%. F. e. s. F. Kurzer, Soc. *1949*, 3434.

Nickel *Ni*

Cleavage of sulfonic acid esters $ROSO_2R' \rightarrow ROH$

Hydrocarbons from sulfonic acid esters ArOTs → ArH

9. *Alkyl esters* of p-toluenesulfonic acid yield the corresponding alcohols on treatment with H_2 and Raney-Ni catalysts (but not with Pd-$BaSO_4$ or Adams' PtO_2); *aryl esters* give the aromatic hydrocarbons. Alkyl and aryl esters of benzylsulfonic acid are rapidly reduced to the hydroxy

compounds, and benzylsulfonic anilides give (with lower yields) anilines.—E: 3-Benzylsulfonyl-1:2,5:6-diisopropylidene-D-glucose hydrogenated in ethanol with Raney-Ni at atmospheric pressure and room temp. for $^1/_4$ hr. → 1:2,5:6-isopropylidene-D-glucose. Y: 100%.—Similarly: p-Tosyl-m-acetamidophenol → acetanilide. Y: 90%. F.e.s. G.W.Kenner and M.A.Murray, Soc. *1949*, S178.

Remaining elements ↑ HO ⇅ Rem

Hydrochloric acid *HCl*

Hydrolysis of phosphoric acid esters $\cdot OPO(OH)_2 \rightarrow \cdot OH$

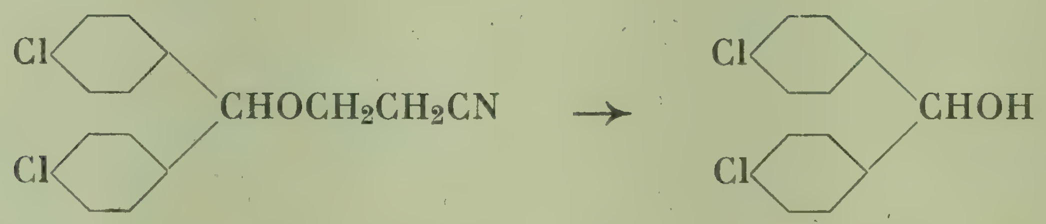
10. Inositol-5-phosphoric acid (prepn. s. 912) with 2 *N* HCl heated in a sealed tube at 130° for 24 hrs. → *meso*-inositol. Crude Y: 91%. B. M. Iselin, Am. Soc. *71*, 3822 (1949).

Carbon ↑ HO ⇅ C

Sodium hydroxide *NaOH*

Cleavage of ethers ROR → ROH

11.



p,p′-Dichlorobenzhydryl-β-cyanoethyl ether refluxed 4 hrs. with 25%-NaOH → p,p′-dichlorobenzhydrol. Y: 97%. O. Grummitt and D. Marsh, Am. Soc. *71*, 4156 (1949); s. a. H. E. Ungnade and K. T. Zilch, J. Org. Chem. *15*, 1108 (1950).

Selective hydrolysis ←
s. *6*, 137

Sodium hydroxide/potassium hydroxide *NaOH/KOH*

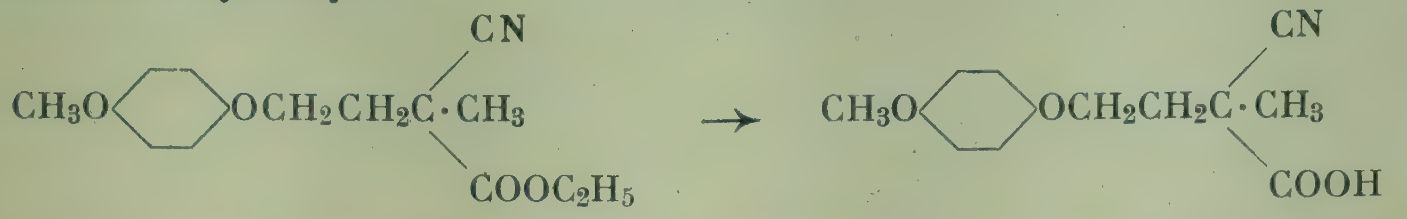
Cleavage of ethers ROR → ROH
s. *6*, 160

Potassium hydroxide *KOH*

Carboxylic acids from carboxylic acid esters COOR → COOH
s. *6*, 136, 689

Selective hydrolysis ←

12.



Ethyl α-cyano-α-methyl-γ-(p-methoxyphenoxy)butyrate (prepn. s. 802) allowed to stand with 1 equivalent of KOH in alcohol-water at room temp. for 6 hrs. → *α-cyano-α*-methyl-γ-(p-methoxyphenoxy)-butyric acid. Y: 89.3%. N. J. Leonard and W. C. Wildman, Am. Soc. *71*, 3089 (1949).

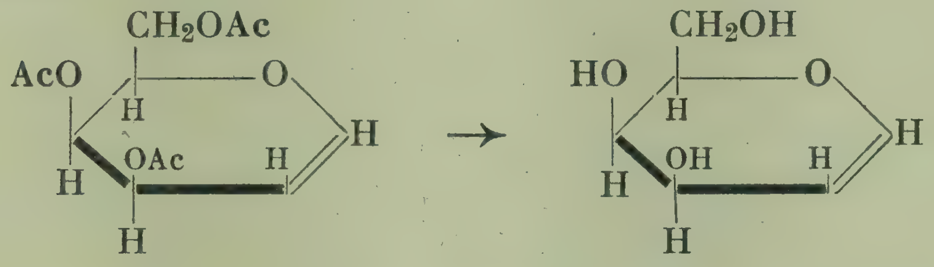
Sodium hydroxide/alcohol

s. *6*, 466

Sodium alkoxide *NaOR*

Deacetylation OAc → OH

13.



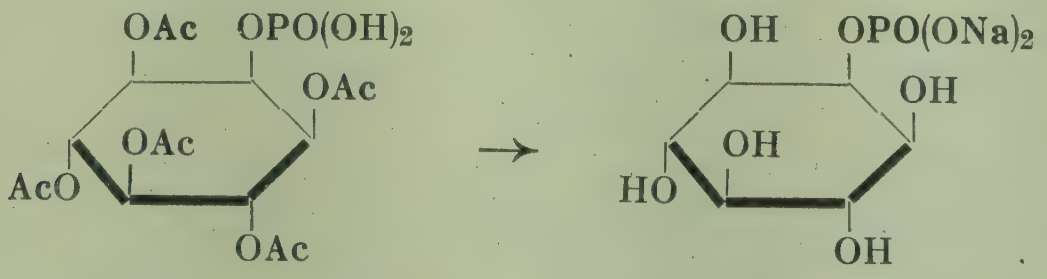
Na added to a soln. of 3,4,6-triacetyl-D-galactal, kept 48 hrs., then solid CO_2 added → D-galactal. Y: 81%.—Deacetylation with $Ba(OH)_2$ gave only 59% yield. W. G. Overend, F. Shafizadeh, and M. Stacey, Soc. *1950*, 671.

. of glycosides

s. *1*, 1; s. a. E. L. May, E. Mosettig, and H. G. Latham, Jr., J. Org. Chem. 15, 890, 884 (1950).

Hydroxyphosphoric acid esters from acetoxyphosphoric acid esters

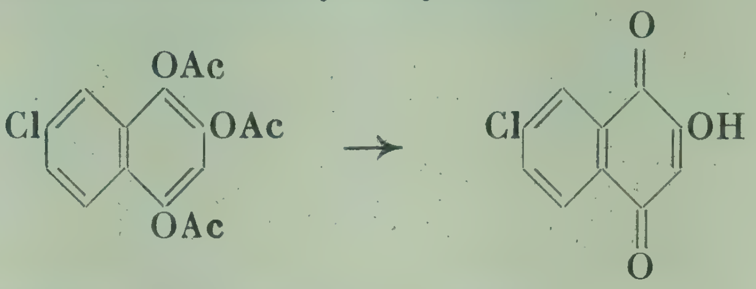
14.



2.5 moles of Na-methoxide in dry methanol added to a methanolic soln. of 1,2,3,4,6-pentaacetylinositol-5-phosphoric acid (prepn. s. 158), and allowed to stand at 0° overnight → Na-inositol-5-phosphate (startg. m. f. 912). Y: 97%. B. M. Iselin, Am. Soc. *71*, 3822 (1949).

Hydroxyquinones from triacoxyisocyclics ←

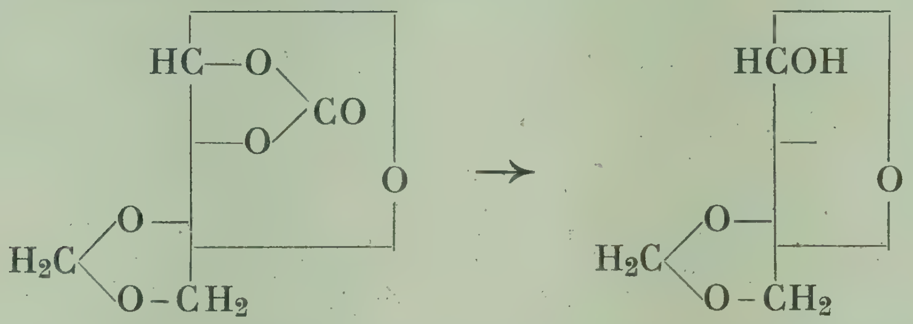
15.



7-Chloro-1,2,4-triacetoxynaphthalene added within 10 min. to a suspension of Na-methoxide in methanol, and stirred 1 hr. in an ice bath in the presence of air → 7-chloro-2-hydroxy-1,4-naphthoquinone. Y: 91%. F. e. s. L. F. Fieser and R. H. Brown, Am. Soc. *71*, 3615 (1949).

Cleavage of carbohydrate carbonates ←

16.



3,5-Monomethylene-D-xylose carbonate in *N*/20 Na-methoxide shaken for 3 hrs., then allowed to stand at room temp. for 3 additional hrs. → 3,5-monomethylene-D-xylose. Y: 92.5 %. O. T. Schmidt and G. Nieswandt, B. *82*, 1 (1949).

Sodium chloride/aluminum chloride s.

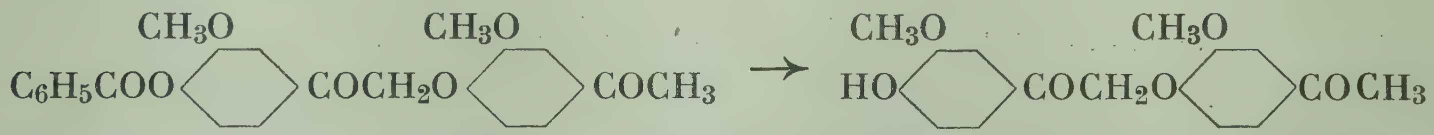
Aluminum chloride/sodium chloride *$NaCl/AlCl_3$*

Piperidine *$C_5H_{11}N$*

Selective hydrolysis
Debenzoylation

OBz → OH

17.



Acetoguaiacyl-acetoguaiacone benzoate refluxed 20 min. with piperidine in alcohol → acetoguaiacyl-acetoguaiacone. Y: 90%. F. e. s. H. Erdtman and B. Leopold, Acta Chem. Scand. *3*, 1358 (1949).

N-Methylmorpholine ←

Partial debenzylation of phosphoric acid esters

$OCH_2C_6H_5 \rightarrow OH$

18. $(C_6H_5CH_2O)_3PO \rightarrow (C_6H_5CH_2O)_2POOH$

Tribenzyl phosphate refluxed 2 hrs. with N-methylmorpholine → dibenzyl hydrogen phosphate. Y: 88%. F. e. s. J. Baddiley et al., Soc. *1949*, 815.

Magnesium hydroxide *$Mg(OH)_2$*

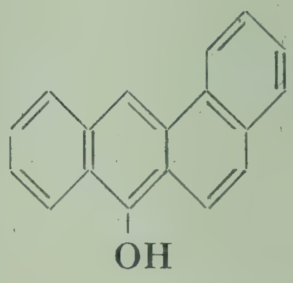
Aldehydes from 1,1-di(acoxy)compounds $CH(OAc)_2 \rightarrow CHO$

19. p-Nitrobenzylidene diacetate refluxed 2 hrs. with a 2.5% suspension of $Mg(OH)_2$ → p-nitrobenzaldehyde. Y: 90-95%. W. Davey and J. R. Gwilt, Soc. *1950,* 204.

Alkyl magnesium halide *RMgHal*

Deacetylation OAc → OH

20.



1,2-Benzanthranyl-10-acetate followed by benzene added to an ethereal soln. of n-butyl-MgBr, the ether allowed to distill, then refluxed for 1 hr. → 1,2-benz-10-anthranol. Y: 84%. L. F. Fieser and E. B. Hershberg, Am. Soc. *59,* 1028 (1937).

Barium methoxide *$Ba(OR)_2$*

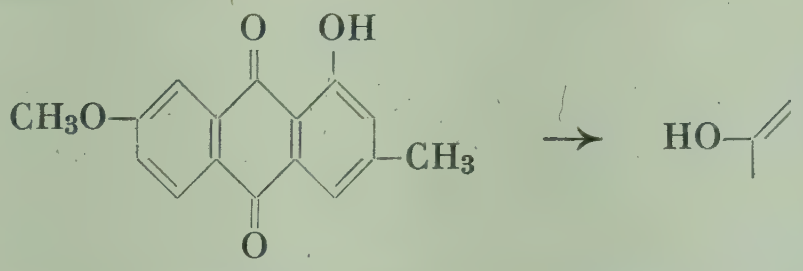
Deacylation of glycosides

s. *1,* 4; *6,* 291; s. a. C. Sannié and H. Lapin, Bl. *1950,* 1234

Aluminum chloride/sodium chloride *$AlCl_3/NaCl$*

Cleavage of ethers ROR → ROH

21.



0.4 gm. 1-hydroxy-3-methyl-7-methoxyanthraquinone ground with $AlCl_3$ and NaCl, then heated at a bath temp. of 170° for 2 hrs. → 0.3 gm. 1,7-dihydroxy-3-methylanthraquinone.—Demethylation with HBr in glacial acetic acid was not successful. H. Mühlemann, Pharm. Acta Helv. *24,* 356 (1949).

Aluminum bromide *$AlBr_3$*

s. *1,* 234; *4,* 14; selective cleavage s. E. H. Ungnade et al., J. Org. Chem. *16,* 64, 70 (1951)

Chymotrypsin

←

Carboxylic acids from carboxylic acid esters COOR → COOH

Enzymatic resolution of racemates

s. *5,* 670; s. a. H. T. Huang and C. Niemann, Am. Soc. *73,* 1541 (1951)

Formic acid *HCOOH*

Carboxylic acids from carboxylic acid esters COOR → COOH
Acidolysis

22. A mixture of methyl acrylate, 98-100%-formic acid, some hydroquinone, and a little H_2SO_4 refluxed 1-3 hrs., then distilled → acrylic acid. Y: 74-78%. C. E. Rehberg, Org. Synth. *29*, 5 (1949).

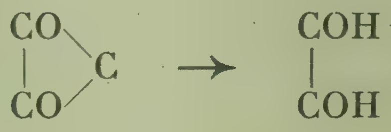
Sulfuric acid *H_2SO_4*

Carboxy-sulfonic acid amides
s. *5*, 14; s. a. Am. Soc. *72*, 2458 (1950)

Hydrochloric acid *HCl*

Enols from enolethers C : C(OR) → C : C(OH)
s. *6*, 320

Cleavage of acetals
s. *6*, 575



of alkyleneacetals
s. *6*, 216

Selective hydrolysis

23. $C_6H_5CH_2CONHCH_2CH(OC_2H_5)_2 \rightarrow C_6H_5CH_2CONHCH_2CHO$

An ethereal soln. of phenylacetylaminoacetal vigorously stirred with aq. NaCl-HCl at room temp. for 4 hrs., neutralized with solid Na-carbonate, and treated with solid CO_2 to chill the soln. and drive off the remaining ether → phenylacetylaminoacetaldehyde hemihydrate. Y: 86%. F. e. s. E. V. Brown, Chemistry of Penicillin *1949*, 482.

24. A soln. of methyl 2,6-dimethanesulfonyl-3,4-isopropyliden-α-D-galactoside in methanol containing some 5 *N* HCl refluxed 2 hrs. → methyl 2,6-dimethanesulfonyl-α-D-galactoside. Y: ca. 100% A. B. Foster et al., Soc. *1949*, 2542.

Deacetylation OAc → OH
s. *6*, 51

Partial deacetylation
of steroid-3-acetoxy groups
s. *2*, 29; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. *72*, 5530 (1950)

Carboxylic acids from carboxylic acid esters

COOR → COOH

25. Concd. HCl added to a soln. of methyl β-ketopalmitate in glacial acetic acid until the soln. becomes slightly turbid, and allowed to stand at room temp. for 48 hrs. → β-ketopalmitic acid. Y: 93%. F. e. s. M. A. Mitz, A. E. Axelrod, and K. Hofmann, Am. Soc. *72*, 1231 (1950).

Hydrobromic acid *HBr*

Cleavage of ethers

ROR → ROH

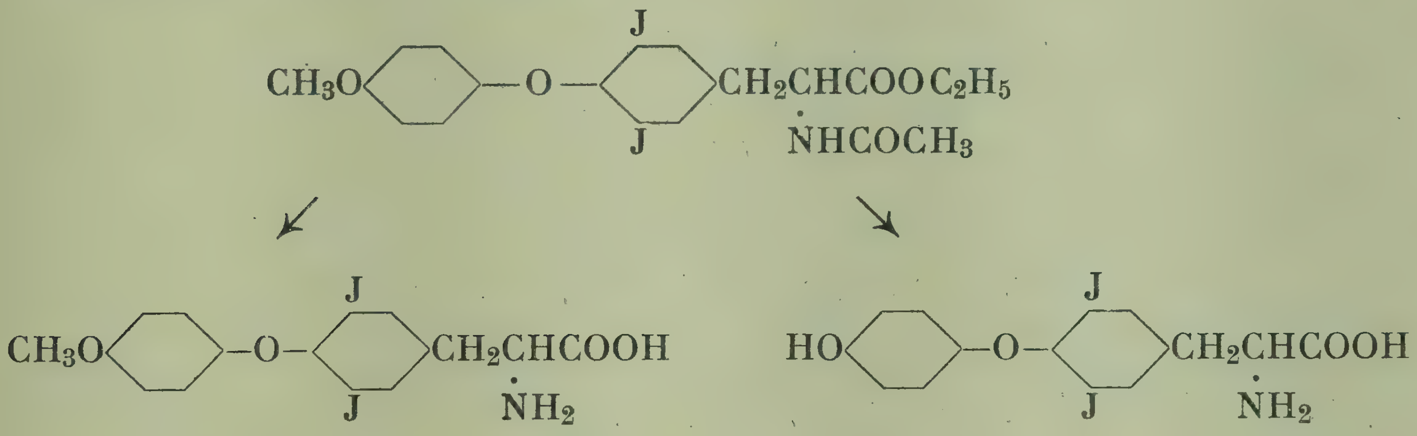
Demethylation s. *1*, 11/2; *2*, 31; *4*, 18; debenzylation s. E. D. Amstutz, Am. Soc. *72*, 3420 (1950)

Hydrochloric and hydriodic acids *HCl and HI*

Selective hydrolysis ←

Optically active compounds

26.



3,5-Diiodo-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester (prepn. s. 592)

refluxed 2 hrs. with a 1:1 mixture of concd. HCl and glacial acetic acid → 3,5-diiodo-4-p-methoxyphenoxy-L-phenylalanine. Y: ca. 100%.	refluxed 4 hrs. in a mixture of 57%-HI and glacial acetic acid → 3,5-diiodo-L-thyronine. Y: 90%.

To avoid racemization, it is preferable to protect the amino group by acetylation and the carboxyl group by esterification rather than by formation of a hydantoin ring. J. R. Chalmers et al., Soc. *1949*, 3424

Hydriodic acid *HI*

Cleavage of ethers

ROR → ROH

27. 3,5-Dimethoxyethylbenzene boiled with HI-acetic acid at 130° for 35 min. → 5-ethylresorcinol. Y: almost 100%. F. e. s. J. P. Brown et al., Soc. *1949*, 859; without acetic acid s. S. V. Sunthankar and H. Gilman, J. Org. Chem. *16*, 8 (1951).

Enols from enolethers C : C(OR) → C : C(OH)
s. *6*, 320

Platinum oxide *PtO₂*

Hydrogenolysis of phosphoric acid esters ←
s. *6*, 158

Formation of H—N Bond

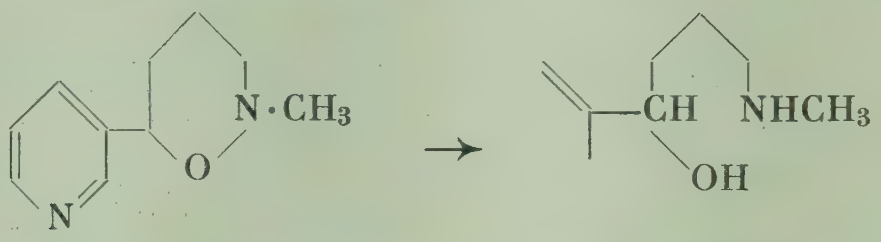
Uptake

Addition to Oxygen and Nitrogen HN ⇓ ON

Zinc *Zn*

Reductive oxazine ring opening C

28.



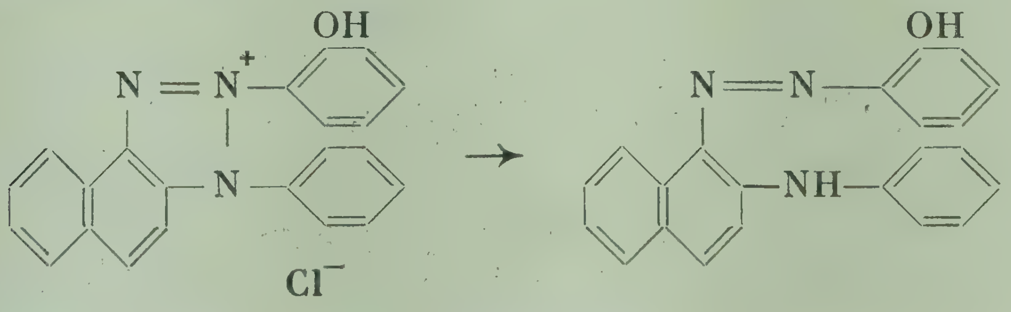
Zn-dust added in small amounts with stirring to a soln. of 2-methyl-6-(3-pyridyl)tetrahydro-1,2-oxazine (prepn., s. 195), in 10%-acetic acid and worked up after 4 hrs. → 4-methylamino-1-(3-pyridyl)-1-butanol. Y: 84.5%. C. H. Rayburn, W. R. Harlan, and H. R. Hanmer, Am. Soc. *72*, 1721 (1950).

Addition to Nitrogen HN ⇓ NN

Sodium hyposulfite *Na₂S₂O₄*

o-Aminoazo compounds from 1,2,3-triazolium salts C

29.



Crude 1-phenyl-2-(o-hydroxyphenyl)naphtho[1,2]triazolium chloride in methanol and some aq. NaOH reduced with Na-hyposulfite at 20° →1-(o-hydroxyphenyl)azo-2-phenylaminonaphthalene. Y: 73%. R. Kuhn and E. Ludolphy, A. *564*, 35 (1949).

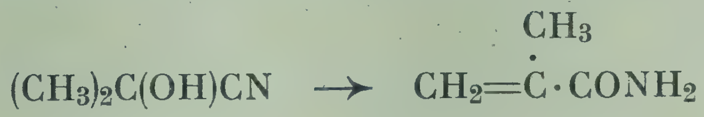
Rearrangement

Hydrogen/Oxygen Type HN⌒HO

Sulfur/sulfuric acid *S/H₂SO₄*

α,β-Ethylenecarboxylic acid amides from cyanohydrins ←

30.



$$(CH_3)_2C(OH)CN \rightarrow CH_2{=}\overset{CH_3}{\dot{C}}\cdot CONH_2$$

Acetone cyanohydrin added with rapid stirring at 75-80° during 25 min. to 98%-H_2SO_4 containing a small quantity of flowers of sulfur, then the temp. raised within 5 min. to 150° with continued stirring, and maintained for 15 min. at this temp. → methacrylamide. Y: 61-70%. R. H. Wiley and W. E. Waddey, Org. Synth. *29*, 61 (1949).

Exchange

Oxygen ↑ HN⇅O

Aluminum amalgam *Al,Hg*

Amines from nitro compounds $NO_2 \rightarrow NH_2$

s. *5*, 20; s. a. C. A. Grob and F. Reber, Helv. *33*, 1776 (1950)

Lithium aluminum hydride *LiAlH₄*

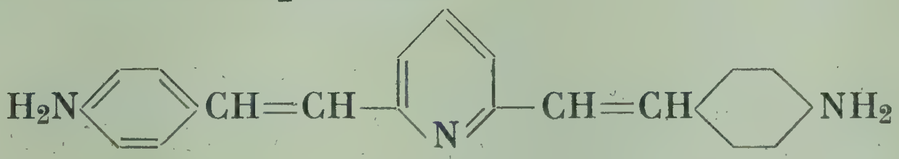
Amines from nitroethylene derivatives ←

s. *6*, 87

Tin *Sn*

Amines from nitro compounds $NO_2 \rightarrow NH_2$

31.



A mixture of 2,6-di-(p-nitrostyryl)pyridine, Sn, and 10%-HCl gently refluxed until the metal has disappeared completely → 2,6-di-(p-aminostyryl)pyridine. Y: 100%.—Hydrogenation with Raney-Ni gave only 49% yield. E. D. Bergmann and S. Pinchas, J. Org. Chem. *15*, 1184 (1950); anmino-γ-pyrones s. E. L. Shimmin and F. Challenger, Soc. *1949*, 1185 who found electrolytic and catalytic reduction methods unsuitable and proceeded according to Ost, J. pr. *19*, 189 (1879); α-amino-β-(allythio)carboxylic acid esters s. 621.

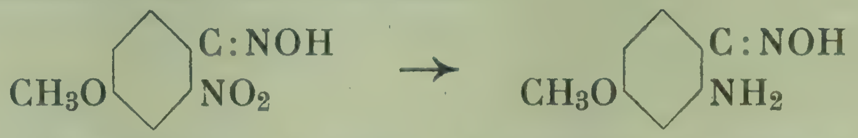
Hydrazine *H₂N·NH₂*

s. *3*, 14; *4*, 71; s. a. L. P. Kuhn, Am. Soc. *73*, 1510 (1951).

Ammonium sulfide $(NH_4)_2S$

Amino-oximes from nitro-oximes

32.



Aq. $(NH_4)_2S$ added to a soln. of 2-nitroanisaldoxime in ethanol, and heated 1 hr. on a water bath → 2-aminoanisaldoxime (startg. m. s. 477). Y: 80%. W. R. Boon, Soc. *1949*, S 230.

Hyposulfite $S_2O_4^{--}$

s. *1*, 360; s. a. M. D. Soffer et al., Am. Soc. *72*, 3704 (1950)

Iron Fe

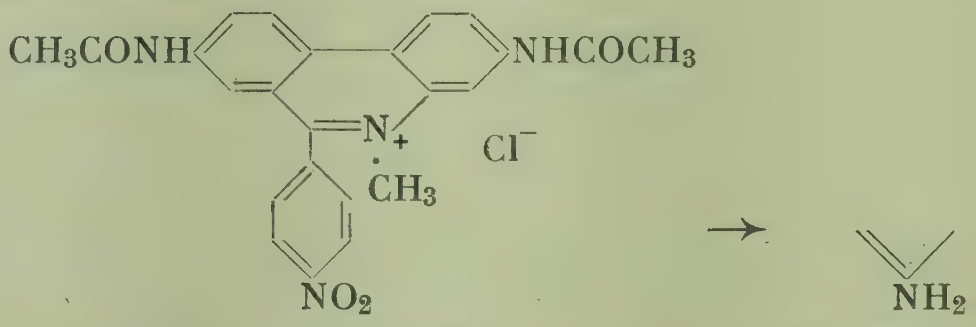
s. *3*, 17; *6*, 820; aliphatic compounds s. G. Tsatsas, Bl. *1949*, 884

simultaneously:
amines from N-oxides
s. *6*, 389

Ferrous sulfate/barium hydroxide $FeSO_4/Ba(OH)_2$

Quaternary aminoammonium salts from quaternary nitroammonium salts

33.



An aq. suspension of $Fe(OH)_2$, prepared from hot aq. soln. of $FeSO_4$ and $Ba(OH)_2$, added to a stirred suspension of 3,8-diacetamido-6-(p-nitrophenyl)-5-methylphenanthridinium chloride in water at 90-95°, heated 30 min. on a steam bath, filtered, the filtrate subjected to further interaction with $Fe(OH)_2$ for 30 min., filtered, and the filtrate treated with NaCl → 3,8-diacetamido-6-(p-aminophenyl)-5-methylphenanthridinium chloride. Y: ca. 100%.— This method proved to be better suited for the reduction of quaternary nitroammonium salts than the reduction with Fe powder. F. e. s. L. P. Walls et al., Soc. *1950*, 41, 311, 2698.

Nickel Ni

s. *1*, 28/9; *2*, 48, 77; *3*, 18/9; aliphatic compounds s. G. B. Butler and F. N. McMillan, Am. Soc. *72*, 2978 (1950)

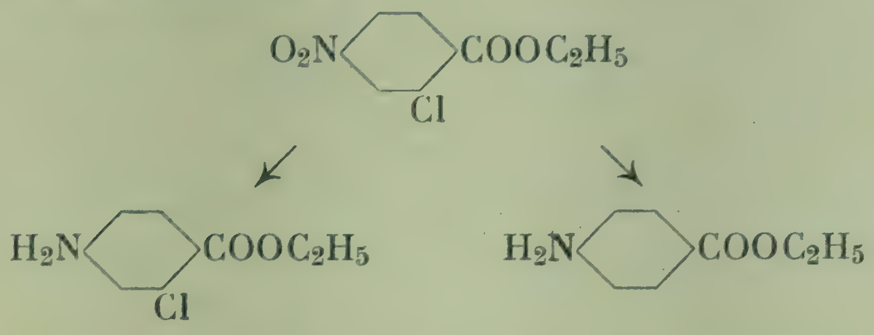
Aminoacetals from nitroacetals

34. m-Nitrobenzaldehyde dimethylacetal hydrogenated with Raney-Ni at 1000-1500 lbs. below 85° → m-aminobenzaldehyde dimethylacetal. Y: 67-78%. R. N. Icke et al., Org. Synth. *29*, 6 (1949).

Palladium-barium sulfate *Pd-BaSO$_4$*

also with simultaneous replacement of chlorine by hydrogen

35.



In the catalytic reduction of 4-nitro-2-chlorobenzoic acid and its esters the chlorine was lost in hydroxylic solvents, but not in ethyl acetate:

Ethyl 4-amino-2-chlorobenzoate hydrogenated with 5%-Pd-BaSO$_4$ at room temp. and atmospheric pressure

in ethyl acetate for 3 hrs. → ethyl 4-amino-2-chlorobenzoate. Y: ca. 100%.	in isopropyl alcohol for 5 hrs. → ethyl 4-aminobenzoate hydrochloride. Y: ca. 100%.

F. e. and side reactions s. A. Weizmann. Am. Soc. *71*, 4154 (1949).

Palladium-barium sulfate/oxalic acid *Pd-BaSO$_4$/(COOH)$_2$*

Aliphatic hydroxylamines from aliphatic nitro compounds

$NO_2 \rightarrow NHOH$

36. $CH_3[CH_2]CH(OH)CH_2NHOH$

A soln. of 1-nitro-2-pentanol and oxalic acid in 95%-alcohol hydrogenated with 5%-Pd-BaSO$_4$ → 1-hydroxylamino-2-pentanol oxalate. Y: 81%. F. e. s. E. Schmidt, A. Ascherl, and L. Mayer, B. *58*, 2430 (1925); s. a. A. Allais, Bl. *1949*, 536.

Platinum *Pt*

Amines from oximes

$C:NOH \rightarrow CHNH_2$

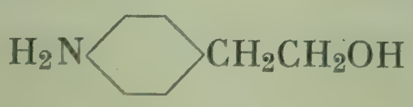
s. *5*, 27; s. a. Bl. *1950*, 627

Platinum and platinum oxide *Pt and PtO$_2$*

Amines from nitro compounds

$NO_2 \rightarrow NH_2$

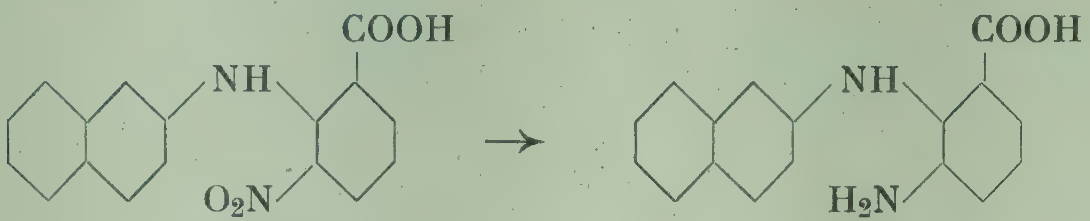
37.



β-(4-Nitrophenyl)ethanol in 95% alcohol hydrogenated with Pt-black at an initial pressure of 50 lbs./sq.in. with intermittent shaking until the calculated amount of H_2 has been absorbed → *β*-(4-aminophenyl) ethanol. Y: 85%. F. e. s. H. M. Woodburn and C. F. Stuntz, Am. Soc. *72*, 1361 (1950); with PtO$_2$ s. A. Dornow and F. Boberg, B. *83*, 261 (1950).

Platinum oxide *PtO_2*

38.



2-(2-Naphthylamino)-3-nitrobenzoic acid hydrogenated with PtO_2 in 96%-alcohol for ca. 2 hrs. → 2-(2-naphthylamino)-3-aminobenzoic acid. Y: 82%.—Phenazine ring closure takes place in the reduction with $SnCl_2$. R. Huisgen and G. Sorge, A. *566*, 162 (1950).

Nitrogen ↑ HN ⇅ N

Without additional reagents *w.a.r.*

Nitroguanidines from N-nitroso-N′-nitroguanidines ←

s. *5*, 28; s. a. R. A. Henry, Am. Soc. *72*, 3287 (1950)

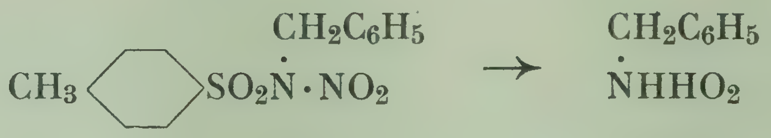
Sulfur ↑ HN ⇅ S

Sodium hydroxide *NaOH*

Cleavage of sulfonic acid amides
N-Nitramines

$N \cdot SO_2R \rightarrow NH$

39.



N-Nitro-N-benzyltoluene-p-sulfonamide refluxed with 0.1 *N* NaOH until complete solution was obtained → benzylnitramine. Y: ca. 90%. F. e. s. M. I. Gillibrand and A. H. Lamberton, Soc. *1949*, 1883.

Carbon ↑ HN ⇅ C

Without additional reagents *w.a.r.*

α-Aminocarboxylic acid amides from oxazolidines ↺

s. *6*, 347

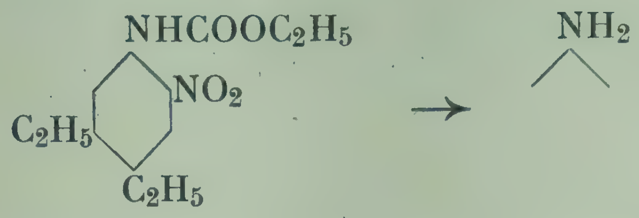
Sodium hydroxide *NaOH*

α-Aminocarboxylic acids from α-formamidomalonic esters ←

s. *6*, 127, 789

Elimination of N-carbethoxy groups N·COOR → NH

40.



4,5-Diethyl-2-nitrocarbethoxyanilide added to aq.-alc. NaOH, the temp. raised to 70° with stirring, and held at this temp. for 1 hr. → 4,5-diethyl-2-nitroaniline. Y: 81%. J. P. Lambooy, Am. Soc. *71*, 3756 (1949).

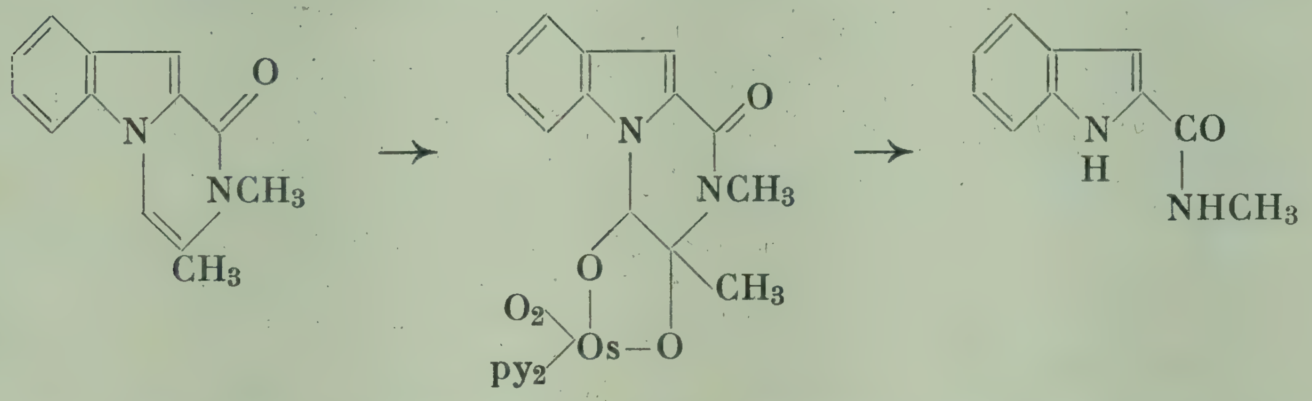
Potassium hydroxide *KOH*

Amines from acylamines NAc → NH
s. *6*, 502

Sodium sulfite *Na_2SO_3*

Pyrazine ring degradation C

41.

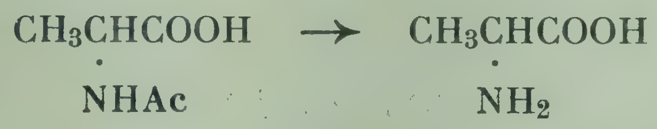


A soln. of 3′-keto-4′,5′-dimethyl-1′,2′,3′,4′-tetrahydropyrazino(1′,2′,1,2)-indole in anhydrous benzene containing pyridine treated with OsO_4, worked up after 3 days, and the pyridine osmiate (Y: high) refluxed 1 hr. with Na-sulfite in alcohol-water → indole-2-carboxymethylamide (Y: 77%). J. A. Elvidge and F. S. Spring, Soc. *1949*, 2935.

Hog kidney enzyme ←

Resolution of racemates by enzymic hydrolysis
Amines from acylamines NAc → NH

42.



$$\underset{NHAc}{CH_3\dot{C}HCOOH} \longrightarrow \underset{NH_2}{CH_3\dot{C}HCOOH}$$

A suspension of hog kidney enzyme preparation (see original paper) added to a mixture of acetyl-DL-alanine in dil. aq. NH_3 at pH 7.9, and kept at 37° for 12 hrs. → L-alanine. Y: 73%. F. e. s. V. E. Price et al., J. Biol. Chem. *178*, 503 (1949); *179*, 1169 (1949); s. a. J. P. Greenstein et al. Am. Soc. *72*, 2812 (1950); J. Biol. Chem. *182*, 452 (1950); C. G. Baker and A. Meister, Am. Soc. *73*, 1336 (1951).

Formic acid *HCOOH*

Amines from isothiocyanates N : C : S → NH_2

43. $(CH_3)_3C\cdot N{=}C{=}S \rightarrow (CH_3)_3C\cdot NH_2$

tert-Butyl isothiocyanate refluxed with 94%-formic acid on a water bath for 80-120 hrs. until the escaping vapors fail to darken Pb-acetate paper → *tert*-butylamine. Y: 79.3%. E. Schmidt et al., A. *568*, 192 (1950).

Formic acid/hydrochloric acid *HCOOH/HCl*

α-Aminocarboxylic acids from α-cyanourethans ←

s. *3*, 189; s. a. Can. J. Research *28 B*, 207 (1950)

Acetic acid *CH_3COOH*

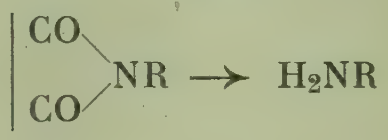
β-Aminoalcohols from oxazolidines

s. *6*, 73

Hydrazine *$H_2N\cdot NH_2$*

Prim. amines from phthalimides

s. *6*, 342



Phosphonium iodide *PH_4I*

Amines from urethans
Cleavage of carbalkoxy derivatives of amines

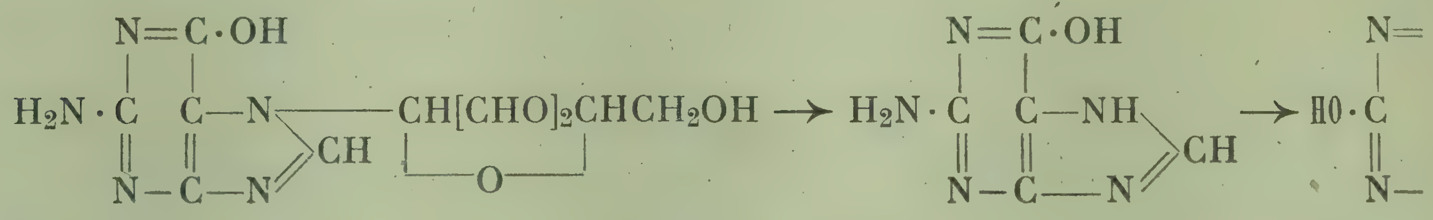
NHCOOR → NH_2

s. *2*, 138; *3*, 25; s. a. C. M. Stevens and R. Watanabe, Am. Soc. *72*, 725 (1950); F. W. Dunn and K. Dittmer, J. Biol. Chem. *188*, 263 (1951)

Sulfuric acid *H_2SO_4*

Cleavage of nucleosides with subsequent replacement of amino groups by hydroxyl ←

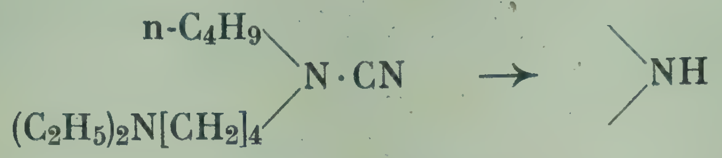
44.



Guanosine boiled 15 min. with H_2SO_4-water, cooled to 85°, and treated dropwise with aq. $NaNO_2$ at 70-80° over a period of 2-3 hrs. → xanthine (startg. m. f. 485). Y: 97%. H. Bredereck, H.-G. v. Schuh, and A. Martini, Chem. B. *83*, 201 (1950).

Amines from cyanamides $N\cdot CN \rightarrow NH$

45.



N-Butyl-δ-diethylaminobutylcyanamide refluxed 15 hrs. with H_2SO_4-water → 1-diethylamino-4-butylaminobutane. Y: 80%.—The cyano group can also be removed by hydrogenolysis with Raney-Ni. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. *14*, 605 (1949).

Hydrochloric acid *HCl*

Elimination of the N-carbethoxy group $N\cdot COOR \rightarrow NH$
s. *6*, 465

Amines from isocyanates $N:C:O \rightarrow NH_2$
s. *6*, 381

Hydrochloric and hydroiodic acids *HCl and HI*

Amines from acylamines
Selective hydrolysis $NAc \rightarrow NH$
s. *6*, 26

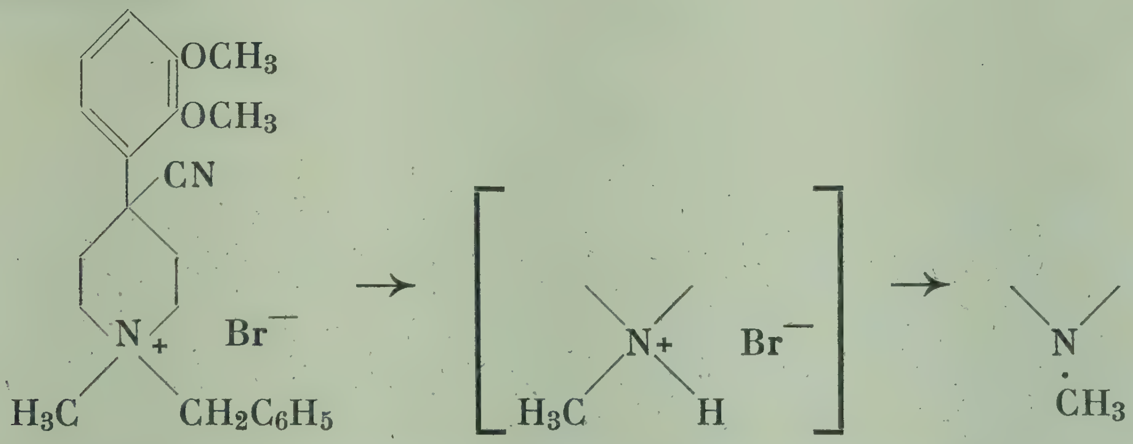
Nickel *Ni*

Amines from cyanamides $N\cdot CN \rightarrow NH$
s. *6*, 45

Palladium *Pd*

Tert. amines from quaternary ammonium salts ←

46.



1-Methyl-1-benzvl-4-o,m-dimethoxyphenyl-4-cyanopyridinium bromide hydrogenated in 50%-alcohol with Pd-black until 1 mole of H_2 is absorbed, the hydrobromide so obtained dissolved in water, and the free base precipitated with Na-carbonate → 1-methyl-4-o,m-dimethoxyphenyl-4-cyanopiperidine. Y: almost 100%. F. e. s. H. Kägi and K. Miescher, Helv. *32*, 2489 (1949).

Palladium-carbon *Pd-C*

Debenzylation $NCH_2C_6H_5 \rightarrow NH$
s. *6*, 364

Formation of H—S Bond

Exchange

Halogen ↑ HS ⇅ Hal

Lithium aluminum hydride *$LiAlH_4$*

Reduction of sulfur compounds $SO_2Cl \rightarrow SH$
Mercaptans from thiocyanates, disulfides, $SCN \rightarrow SH$
and sulfonic acid chlorides $RSSR \rightarrow 2\ RSH$
Sym. disulfides from sulfenyl chlorides $2\ RSCl \rightarrow RSSR$
and thiosulfonates $RSO_2SR \rightarrow RSSR$
Hydrocarbons from sulfonic acid esters $ROSO_2R' \rightarrow RH$

47. Cholesteryl thiocyanate allowed to react with $LiAlH_4$ in ether → 3-mercapto-5-cholestene. Y: 81%.—Similarily: Dicholesteryl disulfide → 3-mercapto-5-cholestene. Y: 88%.—p-Tolyl sulfenylchloride → di-p-tolyl disulfide. Y: 88%.—p-Toluenesulfonyl chloride → p-thiocresol. Y: 90%.—p-Tolyl p-toluenethiosulfonate → di-p-tolyl disulfide. Y: 75%.—3-Cholestanol p-toluenesulfonate → cholestane. Y: 80%.—The reduction of disulfides is very slow. Sulfonamides (in contrast to carbonamides), thioethers, sulfoxides, and sulfones could not be reduced. F. e. s. J. Strating and H. J. Backer, R. *69*, 638, 909 (1950).

Sulfur ↑ HS ⇅ S

Sodium sulfide *Na_2S*

Mercaptans from sym. disulfides $RS{\cdot}SR \rightarrow 2\ RSH$
s. *6*, 660

Zinc *Zn*

48. Concd. HCl and Zn-dust added in portions to a soln. of 2,2′-dichlorodibenzyl disulfide so as to maintain a rapid evolution of H_2, and worked up when a diluted sample formed a clear soln. with aq. NaOH → o-chlorobenzyl mercaptan. Y: ca. 100%. F. e. s. J. W. Boenigk, J. E. Christian, and G. L. Jenkins, J. Am. Pharm. Assoc. *38*, 357 (1949).

Lithium aluminum hydride *$LiAlH_4$*

s. *6*, 47; s. a. R. C. Arnold, A. P. Lien, and R. M. Alm, Am. Soc. *72*, 731 (1950)

Carbon ↑ HS ⇅ C

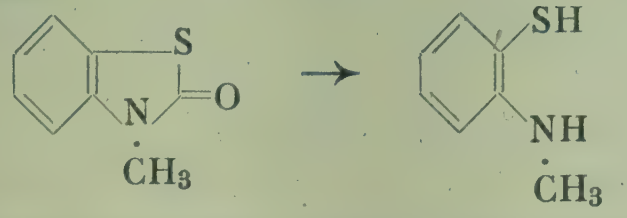
Sodium hydroxide/alcohol *NaOH*

Mercaptans from thiolic acid esters $SCOR \rightarrow SH$
s. *6*, 51

Potassium hydroxide/alcohol *KOH*

Thiazole ring opening C

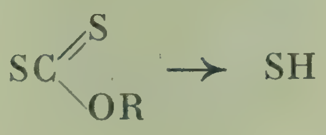
49.



3-Methyl-2(3H)-benzothiazolone boiled 10-20 min. with KOH in alcohol → o-(methylamino)phenyl mercaptan. Y: 84%. F. e. s. A. I. Kiprianov and Z. N. Pazenko, Ж. *19,* 1523 (1949); C. A. *44,* 3487g.

Ammonia *NH_3*

Mercaptans from xanthates



$\mathrm{SC(=S)OR} \rightarrow \mathrm{SH}$

s. *6,* 656

Lithium aluminum hydride *$LiAlH_4$*

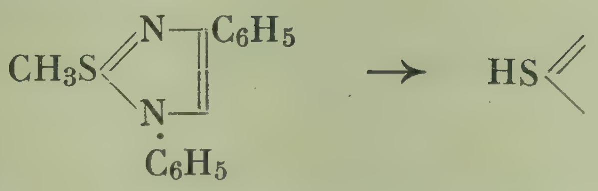
Mercaptans from thiocyanates SCN → SH

s. *6,* 47

Phosphorus/iodine *P/I*

Mercaptans from thioethers RSR → RSH

50.



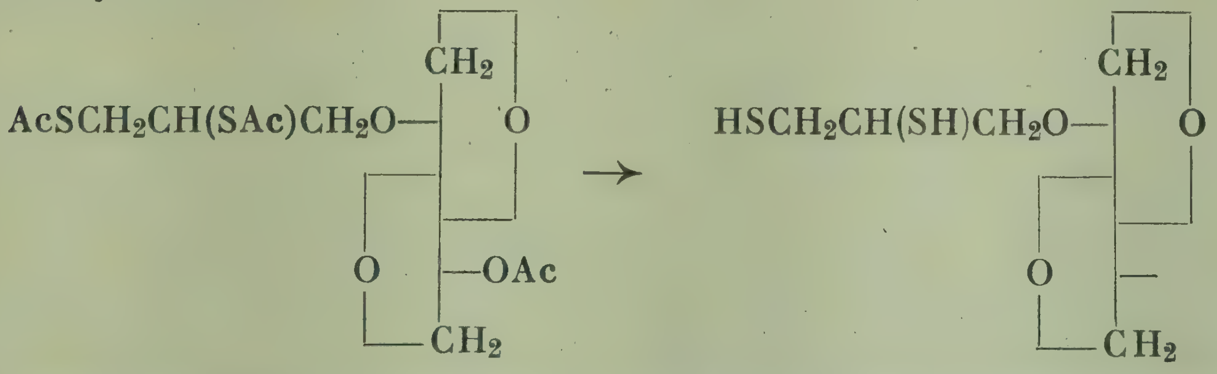
Red P added to iodine in glacial acetic acid, refluxed 20 min., 2-methylthio-1,4-diphenylimidazole added, and refluxed 3.5 hrs. → 1,4-diphenyl-2-thiolimidazole (startg. m. f. 142). Y: 76%. F. e. s. R. M. Dodson and F. Ross, Am. Soc. *72,* 1478 (1950); method, s. Am. Soc. *70,* 2753 (1948).

Hydrochloric acid *HCl*

Mercaptans from thiolic acid esters SCOR → SH

Deacetylation

51.



Triacetyl-2-(2,3-dimercaptopropyl)-1,4:3,6-dianhydromannitol refluxed 4 hrs. under N_2 with 2% methanolic HCl → 2-(2,3-dimercaptopropyl)1,4:3,6-dianhydromannitol. Y: 83%. P. Bladon and L. N. Owen, Soc. *1950,* 591; f. e. s. Soc. *1950,* 579; with NaOH/methanol s. Soc. *1950,* 2943.

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Formation of H—Rem Bond

Exchange

Halogen ↑ **HRem ⇅ Hal**

Lithium aluminum hydride *$LiAlH_4$*

Silanes from halogenosilanes SiHal → SiH

52. $(C_6H_{11})_3SiCl \rightarrow (C_6H_{11})_3SiH$

A soln. of chlorotri(cyclohexyl)silane in anhydrous ether added dropwise to an excess of $LiAlH_4$ in ether, and refluxed 0.5 hr. → tri(cyclohexyl)silane. Y: 90%. W. H. Nebergall and O. H. Johnson, Am. Soc. *71*, 4022 (1949); *72*, 4702 (1950).

Formation of H—C Bond

Uptake

Addition to Oxygen and Carbon HC ⇓ OC

Sodium amalgam *Na,Hg*

Prim. alcohols from aldehydes CHO → CH_2OH

s. *2*, 55; *3*, 32; hydroxycarboxylic acids s. A. S. Elina and O. Y. Magidson, Ж *21*, 780 (1951); C. A. *45*, 9531 d

Lithium boron hydride *$LiBH_4$*

Lactones from ketocarboxylic acids,
nitroalcohols from nitroketones,
and other reductions ←

53. $LiBH_4$ in ether is a more powerful reducing agent than $NaBH_4$ (in water or alcohol) but is milder than $LiAlH_4$. Oxo compounds are reduced rapidly at room temp. in exothermic reactions, whereas esters react slowly and the mixtures must be refluxed for periods up to 6 hrs. In the selective reduction of the carbonyl group ice-bath cooling is employed to enhance selectivity.—E: β-Benzoylpropionic acid → γ-phenylbutyrolactone. Y: 78%.—m-Nitroacetophenone → α-(m-nitrophenyl)ethanol. Y: 93%. F. e. s. R. F. Nystrom, S. W. Chaikin, and W. G. Brown, Am. Soc. *71*, 3245 (1949).

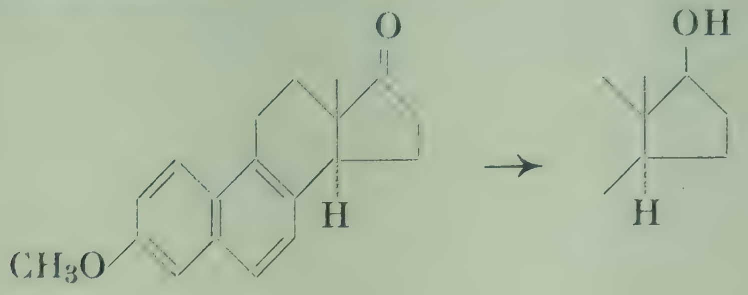
Sodium boron hydride *$NaBH_4$*

Alcohols from oxo compounds CO → CHOH

s. *5*, 40; s. a. J. H. Biel, Am. Soc. *73*, 847 (1951)

Sec. alcohols from ketones

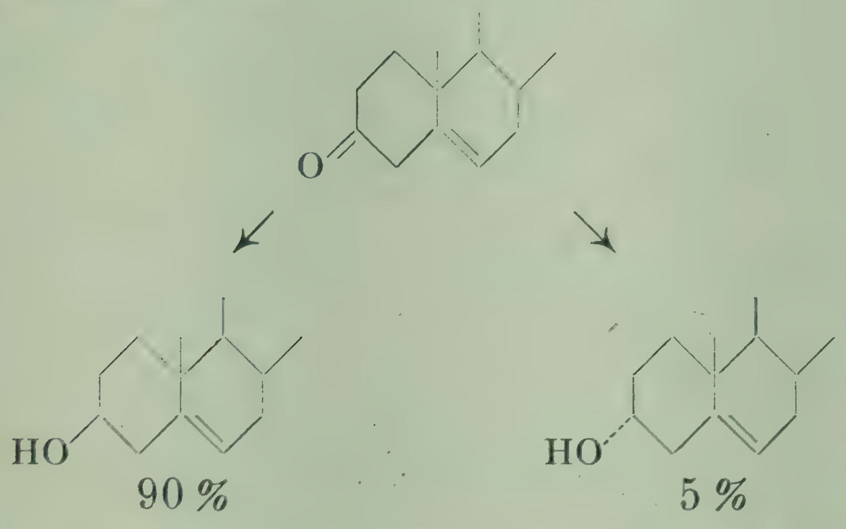
54.



A mixture of d-equilenin methyl ether and $LiAlH_4$ in ether refluxed 3 hrs. → β-dihydroequilenin methyl ether. Y: 97%. W. Bachmann and A. S. Dreiding, Am. Soc. *72*, 1323 (1950); α,β-diaminoalcohols s. N. H. Cromwell and Kwan-Chung Tsou, J. Org. Chem. *15*, 1219 (1950); alcohols from hindered ketones s. E. L. May and E. Mosettig, Am. Soc. *73*, 1301 (1951).

Stereoisomeric steroids

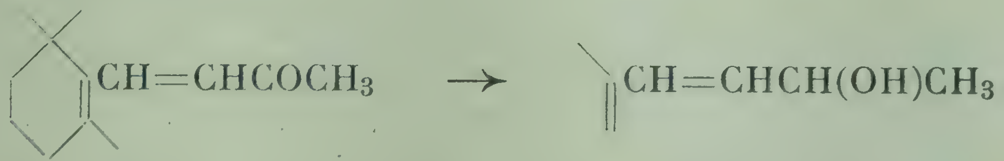
55.



An ethereal soln. of cholest-5-en-3-one added during 25 min. to a vigorously stirred ethereal soln. of $LiAlH_4$, and stirring continued for 2 hrs. with addition of ether from time to time → cholesterol (Y: ca. 90%) and epicholesterol (Y: ca. 5%). F. e. s. C. W. Shoppee and G. H. R. Summers, Soc. *1950*, 687.

Sec. ethylenealcohols from ethyleneketones

56.



β-Ionone in abs. ether dropped into a soln. of $LiAlH_4$ in abs. ether with stirring and ice-cooling over a period of 10 min., and stirring continued at 0° for 1 hr. → β-ionol. Y: almost 100%.—The double bond is not affected at low temp. H. H. Inhoffen, F. and M. Bohlmann, A. *565*, 35 (1949); s. a. V. Boekelheide and C. E. Larrabee, Am. Soc. *72*, 1245, 1240 (1950).

Glycols from α-diketones

57. $C_6H_5COCOC_6H_5 \rightarrow C_6H_5CH(OH)CH(OH)C_6H_5$

Benzil reacted with $LiAlH_4$ in ether
at 35° ↘ ↙ at —80°
meso-hydrobenzoin.
Y: 81%. Y: 90%.

The isomeric composition obtained by this reaction resembles that in catalytic hydrogenation. F. e. s. L. W. Trevoy and W. G. Brown, Am. Soc. *71,* 1675 (1949).

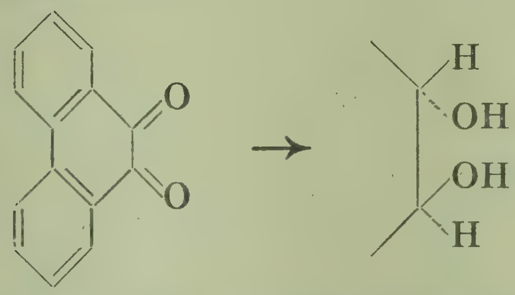
γ-Hydroxyketones from α,β-ethylene-γ-diketones 1,4-Diols from γ-diketones

58. $C_6H_5COCH{=}CHCOC_6H_5 \rightarrow C_6H_5COCH_2CH_2CH(OH)C_6H_5$

10 gm. *cis*- or *trans*-dibenzoylethylene extracted over a period of 5 hrs. from a Soxhlet thimble by refluxing a soln. of 1.5 gm. $LiAlH_4$ in dry ether → 9 gm. 1,4-diphenyl-4-hydroxy-1-butanone and 1 gm. 1,4-diphenylbutane-1,4-dione.—Saturated γ-diketones give diols in good yields. F. e. s. R. E. Lutz and J. S. Gillespie, Jr., Am. Soc. *72,* 2002 (1950).

Dihydroquinols from quinones ←

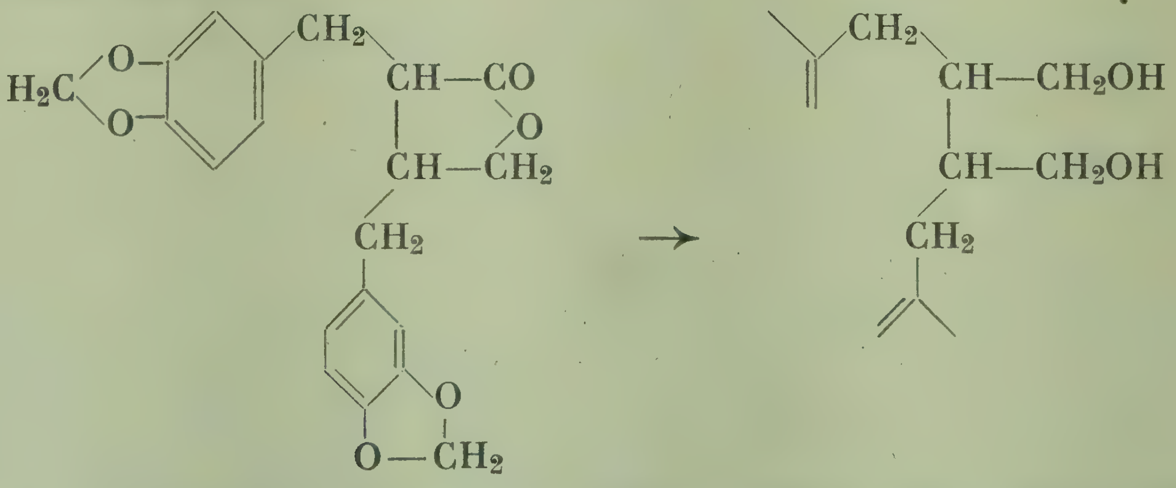
59.



9,10-Phenanthrenequinone extracted in a Soxhlet apparatus with ether containing $LiAlH_4$ → (±)-*trans*-9,10-dihydroxy-9,10-dihydrophenanthrene. Y: over 80%. F. e. s. J. Booth, E. Boyland, and E. E. Turner, Soc. *1950,* 1188.

Diols from lactones C

60.

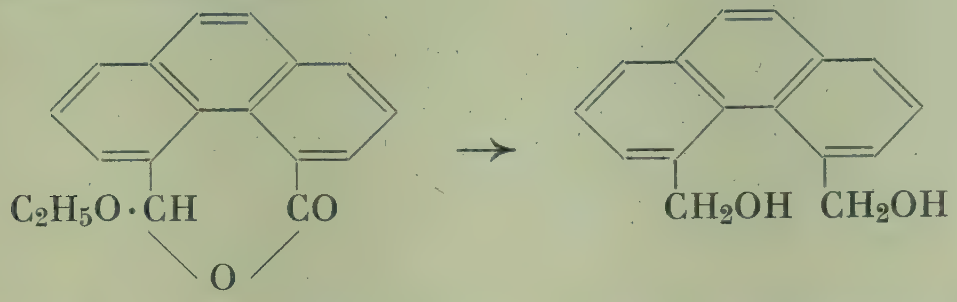


1 gm. (—)-hinokinin in benzene mixed with a soln. of $LiAlH_4$, in ether, and worked up after 2 hrs. → 0.93 gm. (—)-1,4-di-(3,4-methy-

lenedioxyphenyl)-2,3-di(hydroxymethyl)butane. F. e. s. R. D. Haworth and L. Wilson, Soc. *1950*, 71; s. a. C. O. Guss and L. H. Jules, Am. Soc. *72*, 3462 (1950); *73*, 608 (1951); N. L. Drake and E. H. Price, Am. Soc. *73*, 201 (1951).

Diols from alkoxylactones

61.



A warm soln. of pseudo ethyl 5-formyl-4-phenanthrenecarboxylate in benzene added with stirring to an ethereal soln. of $LiAlH_4$ → 4,5-phenanthrenedimethanol (startg. m. f. 302). Y: 90%. M. S. Neuman and H. S. Whitehouse, Am. Soc. *71*, 3664 (1949).

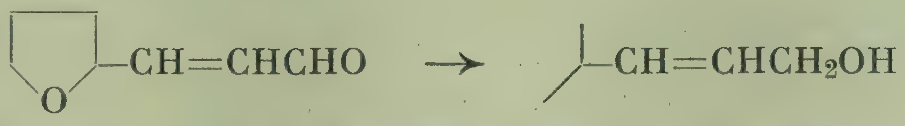
Aluminum alkoxide *Al(OR)$_3$*

Meerwein-Ponndorf reduction

Prim. alcohols from aldehydes

CHO → CH_2OH

62.

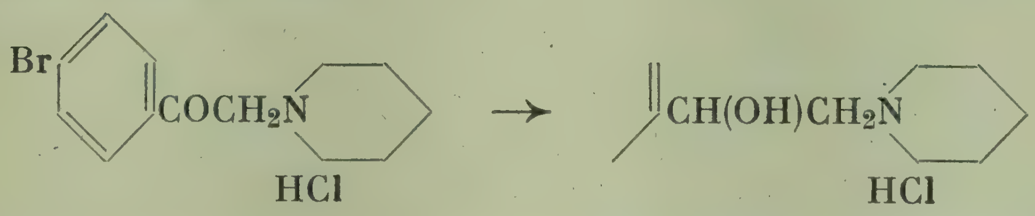


Abs. ethanol added slowly at reflux temp. to coarsely powdered Al, some Al-ethoxide, and xylene, decanted when almost all of the Al is dissolved, the soln. treated with furanacrolein, and heated 2.5 hrs. on a steam bath → 3-(2-furyl)allyl alcohol. Y: 60-70%. M. V. Likhosherstov et al., Ж *20*, 627 (1950); C. A. *44*, 7823d.

Sec. alcohols from ketones

CO → CHOH

63.



Salts of ω-dialkylaminoacetophenones may be reduced directly instead of reducing the free base.—E.: p-Bromo-ω-piperidinoacetophenone hydrochloride, Al-isopropoxide, and benzene slowly distilled with addition of isopropanol until the distillate no longer gives a test for acetone →2-piperidino-1-(p-bromophenyl)ethanol hydrochloride. Y: 89%. F. e. s. D. W. Mathieson and G. Newbery, Soc. *1949*, 1133.

s. a. D. S. Noyce and D. B. Denney, Am. Soc. *72*, 5743 (1950); Ph. Buu-Hoï and H. Khôi, Soc. *1951*, 255
Benzohydrols s. J. P. Picard and C. W. Kearns, Can. J. Research *28B*, 56 (1950)

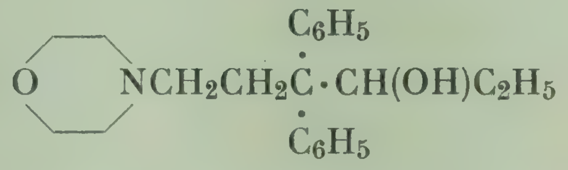
Modified Meerwein-Ponndorf reduction

64. $$C_6H_5CH{=}CHCOCH_3 \rightarrow C_6H_5CH{=}CHCH(OH)CH_3$$

Improved yields of alcohols are obtained from aldehydes and unstable ketones, when the oxo compound is added dropwise during the reaction, so that its concentration is always low.—In certain cases, reductions without solvent may be conveniently employed.—E: A soln. of benzylideneacetone in isopropanol added dropwise within 4.25 hrs., to a refluxing soln. of Al-isopropoxyde distillate collected during the addition at the same rate, and worked up after additional 70 min. → 1-phenylbut-1-en-3-ol. Y: 96%. F. e. s. A. K. Macbeth and J. A. Mills, Soc. *1949*, 2646.

Sec. alcohols from ketones difficult to reduce

65.



1-(4-morpholinyl)-3,3-diphenylhexan-4-one and Al-isopropoxide heated in dry toluene at a bath-temp. of 140—150°, with slow distillation at intervals and addition of more toluene as required, until after ca. 100 hrs. the Na-nitroprusside test for acetone is negative → 1-(4-morpholinyl)-3,3-diphenylhexan-4-ol. Y: 80-90%. A. H. Beckett and W. H. Linnell, J. Pharm. Pharmacol. *2*, 418 (1950).

Stereoisomeric cyclic alcohols from cyclic ketones

66. When cyclic ketones are reduced with Al-alkoxides, the proportion of *cis*-isomer is greatest from ketones and reducing alcohols in which steric hindrance is greatest. L. M. Jackman, A. K. Macbeth, and J. A. Mills, Soc. *1949*, 2641.

Copper chromite *$CuCr_2O_4$*

Alcohols from oxo compounds $CO \rightarrow CHOH$

s. *6*, 108

Prim. alcohols from aldehydes $CHO \rightarrow CH_2OH$

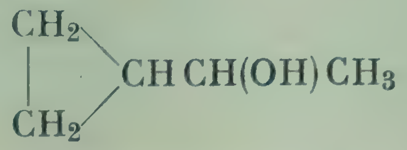
s. *6*, 107; s. a. E. R. Shepard and J. F. Noth, Am. Soc. *72*, 4364 (1950)

Sec. alcohols from ketones $CO \rightarrow CHOH$

s. *3*, 36; large batches s. D. T. Mowry and E. L. Ringwald, Am. Soc. *72*, 2037 (1950)

Barium copper chromite *$(Ba,Cu)Cr_2O_4$*

67.



Methyl cyclopropyl ketone hydrogenated with Ba-promoted copper chromite catalyst at 100° and an initial pressure of 1750 p. s. i./room temp., for ca. 9 hrs., the H_2-absorption beginning after an induction period of ca. 5 hrs. → methylcyclopropylcarbinol. Y: 90%.—Other methods gave lower yields. V. A. Slabey and P. H. Wise, Am. Soc. *71,* 3252 (1949).

Nickel *Ni*

Prim. alcohols from aldehydes

CHO → CH_2OH

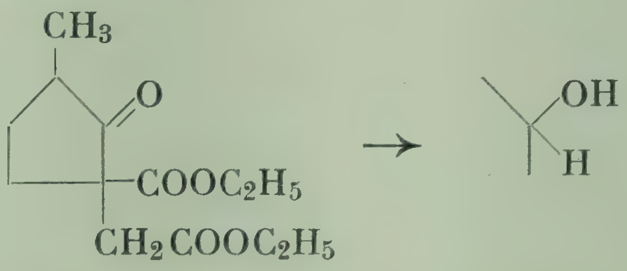
68. $(C_2H_5)_2NCH_2C(CH_3)_2CHO \rightarrow (C_2H_5)_2NCH_2C(CH_3)_2CHOH$

100 gm. α-diethylaminomethylisobutyraldehyde hydrogenated with Raney-Ni in aq. HCl at pH 3-6, 150 lbs. pressure, and 79-80° → 80-90 gm. γ-diethylamino-β,β-dimethylpropanol.—Other reaction conditions and catalysts were unsatisfactory. F. e. s. W. Wenner, J. Org. Chem. *15,* 301 (1950), s. a. E. L. Eliel, Am. Soc. *73,* 43 (1951).

Sec. alcohols from ketones

CO → CHOH

69.



5.5 gm. ethyl 2-carbethoxy-5-methylcyclopentan-1-one-2-acetate in ethanol stirred under H_2 with Raney-Ni at 100°/50 atm. for 6 hrs. → 5.0 gm. ethyl 2-carbethoxy-5-methylcyclopentan-1-ol-2-acetate.—The reduction with Al,Hg and Al-isopropoxide did not succeed. L. N. Owen, Soc. 1949, 1582.

Cyclic sec. alcohols from cyclic ketones
Elimination of the induction period

70. Cyclopentanone hydrogenated at 100 atm. and 130-140° with Raney-Ni for 1 hr. → cyclopentanol. Y: 90%. An induction period of 6-7 hrs. is avoided by adding a little cyclopentanol at the start. G. E. McCasland and D. A. Smith, Am. Soc. *72,* 2190 (1950).

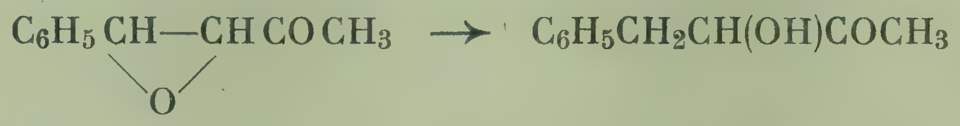
γ-Hydroxypiperidines from γ-pyridones

s. *6,* 90

Nickel/palladium *Ni/Pd*

α-Hydroxyketones from α,β-oxidoketones ←

71.



Benzylideneacetone oxide hydrogenated with Ni (activated by $PdCl_2$) in ethanol at atmospheric pressure and room temp. for ca. 0.5 hr. → benzyl acetyl carbinol. Y: 80%. T. I. Temnikova and V. A. Kropachev, Ж *19*, 2069 (1949); C. A. *44*, 3941c; Ж *21*, 501 (1951); C. A. *45*, 8447c.

Palladium/sulfuric acid or sodium hydroxide *Pd/H_2SO_4 or Pd/NaOH*

Sec. alcohols from ketones CO → CHOH

72. $C_6H_5COCH_3 \rightarrow C_6H_5CH(OH)CH_3$

Conditioning of catalysts. Catalysts, e. g. palladium and platinum, can be activated by treating with acids and again deactivated by addition of bases. Certain hydrogenations can best be performed by such an activated-deactivated catalyst. E: Acetophenone with Pd-black, prepared according to Willstätter and Waldschmidt-Leitz, B. *54*, 123 (1921) and treated with H_2SO_4, hydrogenated in methanol in the presence of a trace of NaOH at 2.5 atm. and room temp. → α-phenylethyl alcohol. Y: 93%. K. Kindler, E. Schärfe, and P. Henrich, A. *565*, 51 (1949).

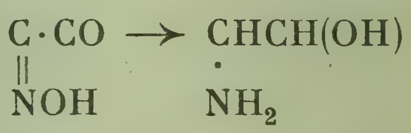
Palladium-carbon *Pd-C*

s. *4*, 55; correction s. W. R. Nes and A. Burger, Am. Soc. *72*, 5409 (1950)

Platinum dioxide *PtO_2*

α-Aminoalcohols from α-isonitrosoketones

s. *6*, 79



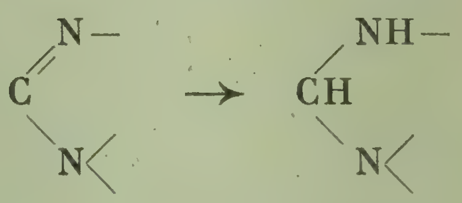
$\underset{\underset{NOH}{\parallel}}{C}\cdot CO \rightarrow \underset{NH_2}{CH}CH(OH)$

Addition to Nitrogen and Carbon HC⇓NC

Aluminum amalgam *Al,Hg*

1,1-Diamines from amidines

s. *6*, 237



Lithium aluminum hydride *$LiAlH_4$*

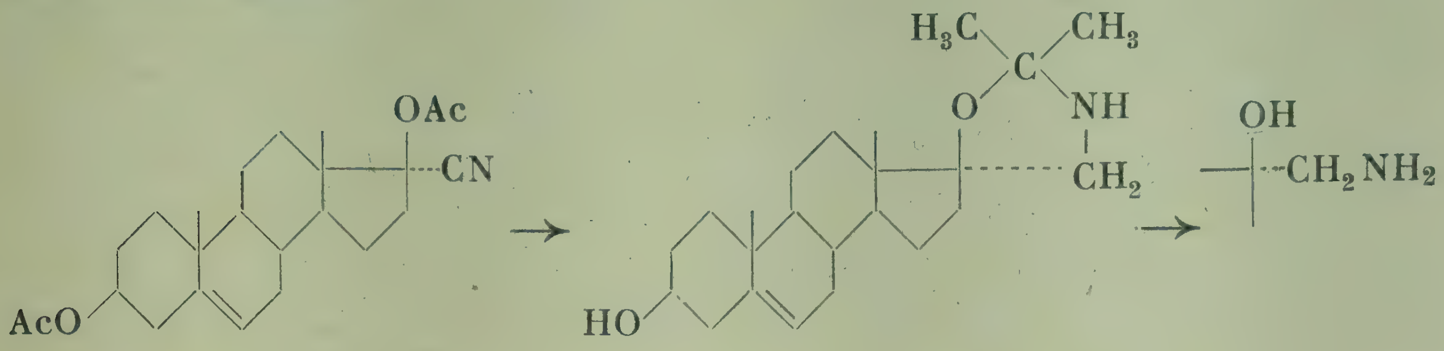
Amines from nitriles CN → CH_2NH_2

s. *4*, 60; s. a. L. H. Amundsen and L. S. Nelson, Am. Soc. *73*, 242 (1951)

β-Aminoalcohols from cyanohydrin acetates via oxazolidines

$CN \rightarrow CH_2NH_2$

73.

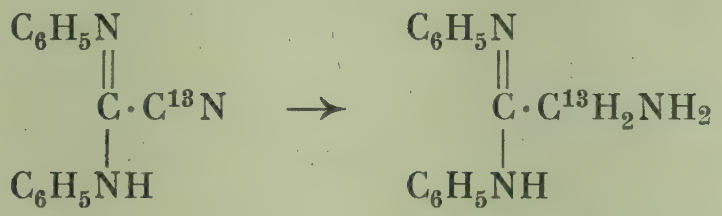


$LiAlH_4$ in ether added dropwise with good stirring to a soln. of $\Delta^{5,6}$-3β,17β-diacetoxy-17-isoetiocholenic acid nitrile, stirring continued for 0.5 hr. at room temp. and for an additional 0.5 hr. at 40°, and worked up whereby the reaction product is extracted with acetone → oxazolidine derivative (Y: over 90%), 100 mg. of which in glacial acetic acid treated with water → 93 mg. $\Delta^{5,6}$-3β,17β-dihydroxy-17α-aminomethylandrostene.—Side reactions are avoided by reducing the cyanohydrin acetate in place of the free cyanohydrin. H. Heusser et al., Helv. *33*, 1093 (1950).

Aminoacetamidines from cyanoformamidines
Labeled compounds

←

74.



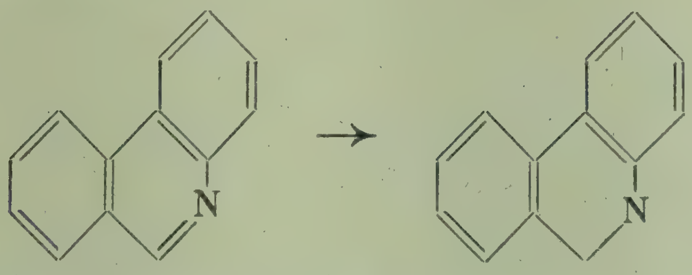
$$C_6H_5N{=}C(C{\cdot}{}^{13}N)(NHC_6H_5) \rightarrow C_6H_5N{=}C(C{\cdot}{}^{13}H_2NH_2)(NHC_6H_5)$$

A soln. of crude, but alcohol-free N,N′-diphenylcyanoformamidine (prepn. s. 824) in anhydrous ether added to $LiAlH_4$ in anhydrous ether in a slow N_2 stream during ca. 2 hrs., at a rate to maintain gentle refluxing → (N,N′-diphenyl)aminoacetamidine (startg. m. s. 230). Y: 65-70%. G. Ehrensvärd and R. Stjernholm, Acta Chem. Scand. *3*, 971 (1949).

Selective ring hydrogenation

←

75.



Phenanthridine introduced by use of a Soxhlet extractor into a well-stirred soln. of $LiAlH_4$ in anhydrous ether over a period of 10 hrs → 5,6-dihydrophenanthridine. Y: 74%. W. C. Wooten and R. L. McKee, Am. Soc. *71*, 2946 (1949).

Cobalt *Co*

Amines from nitriles CN → CH_2NH_2

76. 3,4-Methylenedioxybenzyl cyanide (prepn. s. 812) hydrogenated with 5% Raney-Co in dioxane at 125-150° and an initial pressure of 200 atm./room temp. for ca. 15 min. → homopiperonylamine. Y: 79-87%. —Raney-Ni gives only 50% yield under these conditions. W. Reeve and W. M. Eareckson, 3rd, Am. Soc. *72*, 3299 (1950); s. a. H. F. Piepenbrink, A. *572*, 83 (1951).

Nickel *Ni*

Amines from cyclic imines

77. Cycl. N-subst. imines do not undergo ring fission under the same conditions as the N-unsubst. compounds. H. Bestian, A. *566*, 210 (1950).

Nickel/potassium hydroxide *Ni/KOH*

Amines from nitriles CN → CH_2NH_2

78. $C_6H_5CH_2CN \rightarrow C_6H_5CH_2CH_2NH_2$

Phenylacetonitrile hydrogenated in alcohol with Raney-Ni in the presence of KOH at 55 atm. and 60° for 1 hr. → phenylethylamine. Y: 93%.—The yields are lower in the absence of KOH. F. e. s. M. Métayer, A. ch. [12] *4*, 198 (1949).

Palladium-carbon/sulfuric acid *Pd-C/H_2SO_4*

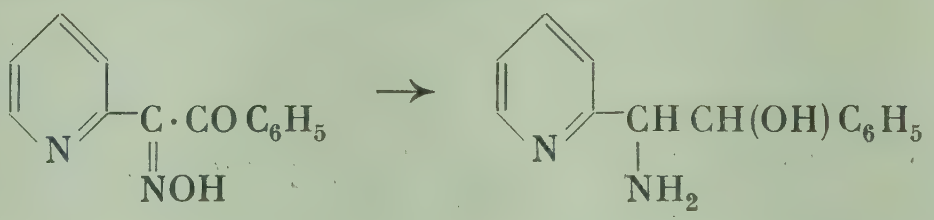
Amines from cyanocarbonates
Directing the hydrogenation by acids
s. *6*, 111

Platinum oxide *PtO_2*

Amines from hydrazones C:NNHR → $CHNH_2$
s. *3*, 39; H. S. Anker, J. Biol. Chem. *187*, 167 (1950)

α-Aminoalcohols from α-isonitrosoketones ←

79.

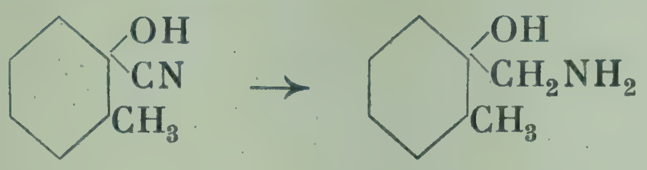


Isonitroso-α-phenacylpyridine in alcohol hydrogenated with PtO_2 at room temp. and atmospheric pressure → 2-amino-1-phenyl-2-(α-pyridyl)-ethanol. Y: 85%.—In glacial acetic acid, hydrogenation of the pyridine nucleus also occurs. F. e. s. A. Dornow and K. Bruncken, Chem. B. *83*, 189 (1950).

Platinum oxide/hydrochloric acid *PtO_2/HCl*

α-Aminoalcohols from cyanohydrins $CN \rightarrow CH_2NH_2$

80.



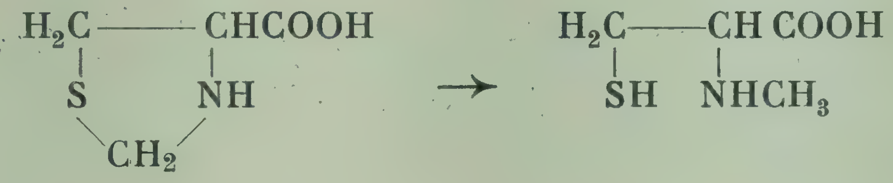
1-Cyano-2-methyl-1-cyclohexanol hydrogenated in acetic acid with PtO_2 in the presence of HCl until the theoretical amount of H_2 is absorbed after 6-7 hrs. → 1-aminomethyl-2-methyl-1-cyclohexanol. Y: 85%. A very active PtO_2 catalyst partially poisoned by inhibitors e. g. CS_2, HCl, HCN, gives an optimum rate of hydrogenation and best yields. F. e. s. B. Tschoubar, Bl. *1949*, 160.

Addition to Sulfur and Carbon HC ⇓ SC

Sodium/liq. ammonia *Na/NH_3*

Reductive thiazolidine ring opening C

81.



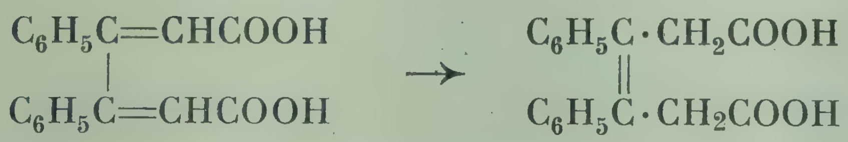
L-Thiazolidine-4-carboxylic acid and Na added alternately in small portions with stirring to liq. NH_3 until a permanent blue color results, which is discharged with a small lump of Dry Ice, NH_3 allowed to evaporate, finally in vacuo, and the residue taken up in water → N-methyl-L-cysteine. Y: 78%. F. e., with lower yields, s. H. M. Crooks, Jr., Chemistry of Penicillin *1949*, 455.

Addition to Carbon HC ⇓ CC

Electrolysis ↯

Partial reduction of dienes to ethylene derivatives $C:C \rightarrow CHCH$

82.



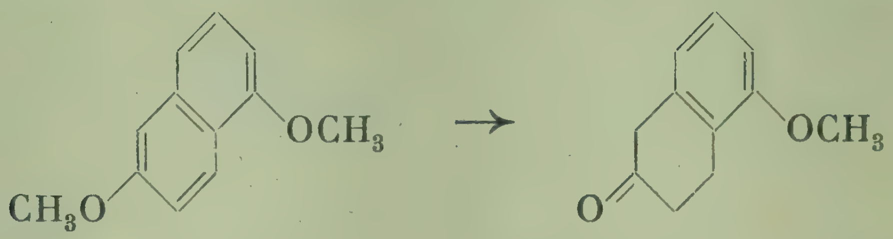
$$\begin{array}{l}C_6H_5C{=}CHCOOH\\ \quad\;|\\ C_6H_5C{=}CHCOOH\end{array} \longrightarrow \begin{array}{l}C_6H_5C\cdot CH_2COOH\\ \quad\;\|\\ C_6H_5C\cdot CH_2COOH\end{array}$$

A soln. of Na-diphenylmuconate in NaOH electrolyzed with a Hg-cathode, 0.02 amp./sq.cm. and 4 amp.-hrs. → dihydrodiphenylmuconic acid. Y: 81%. H. E. Fierz-David, L. Blangey, and M. Uhlig, Helv. *32*, 1414 (1949).

Sodium *Na*

Cylic ketones from phenolethers ←

83.



Na added during 35 min. to a soln. of 225 gm. crude 1,6-dimethoxynaphthalene in boiling alcohol, after addition of more alcohol refluxing continued for ca. 40 min. until the metal has disappeared → 5-methoxy-2-tetralone. Y: ca. 75%. J. W. Cornforth and R. Robinson, Soc. *1949*, 1855; s. a. M. D. Soffer et al., Am. Soc. *72*, 3704 (1950).

Hydrogenation of N-heterocyclic rings

s. *2*, 71; s. a. W. Gruber and K. Schlögl, M. *80*, 499 (1949)

Sodium amalgam *Na,Hg*

Hydrogenation of ethylene derivatives C:C → CHCH

s. *3*, 610; s. a. J. Org. Chem. *14*, 915 (1949); L. J. Owen and F. F. Nord, J. Org. Chem. *15*, 988 (1950)

Lithium/N-methylaniline *Li/$C_6H_5NHCH_3$*

Partial reduction of dienes to ethylene derivatives

84. Cycloöcta-1,3-diene, N-methylaniline, and Li in abs. ether mechanically shaken for 1 day → *cis*-cycloöctene. Y: almost 100%. K. Ziegler and H. Wilms, A. *567*, 1 (1950); s. a. A. *511*, 83 (1934); *528*, 111 (1937).

Sodium/liq. ammonia *Na/NH_3*

Hydrocarbons from *a,β*-ethylenealcohols ←
s. *6*, 138

Sodium/liq. ammonia/alcohol

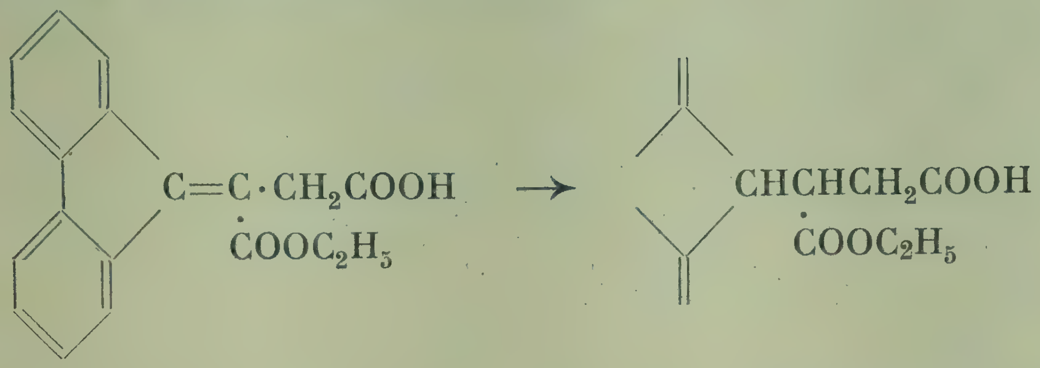
Reduction by dissolving metals ←
Partial ring hydrogenation

s. *5*, 47; s. a. Soc. *1950*, 1551

Zinc *Zn*

Hydrogenation of ethylene derivatives $C:C \rightarrow CHCH$

85.



A soln. of 1 gm. β-carbethoxy-β-fluorenylidenepropionic acid in glacial acetic acid refluxed with Zn dust for 1 hr. → 0.91 gm. β-carbethoxy-β-9-fluorenylpropionic acid. F. e. s. N. Campbell and A. E. S. Fairfull, Soc. *1949*, 1102; s. a. L. J. Owen and F. F. Nord, J. Org. Chem. *15*, 988 (1950).

Zinc/pyridine/acetic acid *$Zn/C_5H_5N/CH_3COOH$*

Partial reduction of dienes to ethylene derivatives

86. $CH_3COCH{=}CHCH{=}CHCOCH_3 \rightarrow CH_3COCH_2CH{=}CHCH_2COCH_3$

3,5-Octadiene-2,7-dione dissolved with warming in dry pyridine, Zn-dust added, followed by glacial acetic acid, and shaken vigorously → 4-octene-2,7-dione. Y: 70-75%. P. Karrer and C. H. Eugster, Helv. *32*, 1934 (1949).

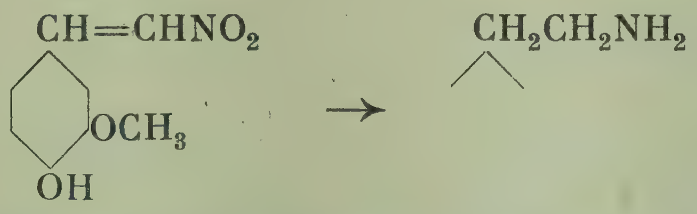
Lithium aluminum hydride *$LiAlH_4$*

γ-Hydroxyketones from α,β-ethylene-γ-diketones ←

s. *6*, 58

Amines from nitroethylene derivatives ←
Soxhlet extractor technique

87.



4-Hydroxy-3-methoxy-β-nitrostyrene (prepn. s. 754) added by the Soxhlet extractor technique (cf. Nystrom and Brown, Am. Soc. *69*, 1197 (1947); Synth. Meth. *6*, 58, 75) to a well-stirred mixture of $LiAlH_4$ and abs. ether over a period of 59 hrs., and the reaction product isolated as picrate → 4-hydroxy-3-methoxyphenylethylamine. Y: 80%. F. e. s. F. A. Ramirez, A. Burger, and M. Erne, Am. Soc. *72*, 2781 (1950); Helv. *33*, 912 (1950); s. a. J. Finkelstein, Am. Soc. *73*, 550 (1951); cf. R. T. Gilsdorf and F. F. Nord, J. Org. Chem. *15*, 807 (1950).

Formic acid *HCOOH*

Amines from enamines C : C → CHCH

88. $CH_3[CH_2]_5CH{=}CHN(CH_3)_2 \rightarrow CH_3[CH_2]_5CH_2CH_2N(CH_3)_2$

87%-formic acid added dropwise with stirring to 1-octenyldimethylamine, then warmed 1-2 hrs. at 50-70° → octyldimethylamine. Y: 92%. F. e. s. P. L. DeBenneville and J. H. Macartney. Am. Soc. *72*, 3073 (1950).

Phosphorus *P*

Hydrogenation of ethylene derivatives
s. *6*, 762

Phosphorus/hydriodic acid *P/HI*

α-Aminocarboxylic acids from thiazolidones
s. *6*, 269

Copper chromite *$CuCr_2O_4$*

Alcohols from ethylene ketones ←
Selective hydrogenation

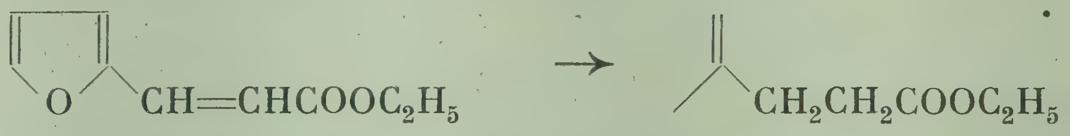
s. *5*, 491; s. a. Am. Soc. *72*, 5506 (1950)

Alcohols from ethylenecarboxylic acid esters ←
s. *6*, 109

Dicobalt octacarbonyl *$Co_2(CO)_8$*

Hydrogenation of ethylene derivatives C : C → CHCH

89.



$Co_2(CO)_8$-catalyst is effective for the hydrogenation of the carbon carbon double bond in certain α,β-ethylenic carbonyl compounds. The yields with the aldehydes were 40-50% while with the ketones and esters they were in the range of 70-90%.—E: 37 gm. ethyl β-(2-furan)-acrylate and dicobalt octacarbonyl in benzene, under a pressure of 4700 p. s. i. of equal parts of H_2 and CO at 125° rocked for 6.5 hrs. → 34.3 gm. ethyl β-(2-furan)propionate.—Hydroformylation of other ethylene derivatives with the same reagent s. Synth. Meth. *4*, 667. H. Akins and G. Krsek, Am. Soc. *71*, 3051 (1949).

Nickel *Ni*

Selective hydrogenation of the carbon carbon double bond

s. *6,* 761; s. a. E. and F. Berliner, Am. Soc. *72,* 222 (1950)

cis-trans-Isomeric ethylene derivatives from acetylene derivatives C ⁝ C → CH : CH

s. *1,* 59/60; s. a. W. R. Taylor and F. M. Strong, Am. Soc. *72,* 4263 (1950); C. S. Marvel and C. H. Young, Am. Soc. *73,* 1066 (1951)

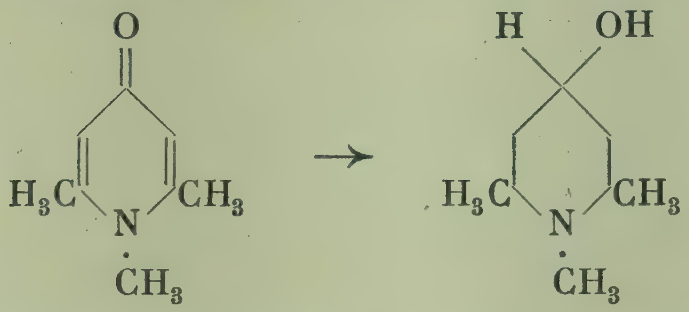
Ring hydrogenation ←

s. *4,* 98; of amines s. M. Métayer, A. ch. *4,* 196 (1949)

Hydrogenation of N-heterocyclic rings

γ-Hydroxypiperidines from γ-pyridones

90.



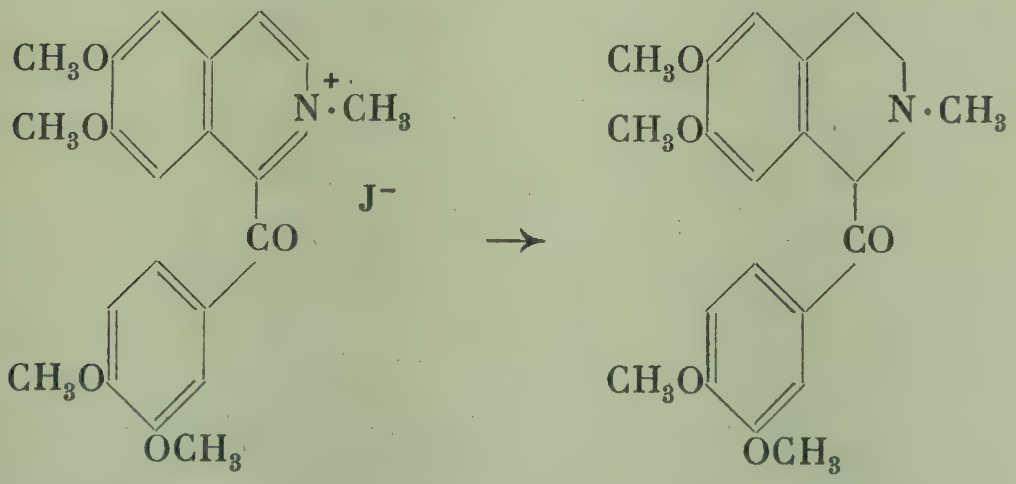
A mixture of 1,2,6-trimethyl-4-pyridone, abs. alcohol, and Raney-Ni hydrogenated at 130 atm. and 125° for 4 hrs. → 1,2,6-trimethyl-4-piperidinol. Y: 85%. F. e. s. K. N. Campbell, J. F. Ackerman, and B. K. Campbell, J. Org. Chem. *15,* 337 (1950).

Piperidones from pyridones

s. *6,* 95

Selective hydrogenation of cyclic quaternary ammonium salts

91.



1-(4,5-Dimethoxybenzoyl)-6,7-dimethoxyisoquinoline methiodide hydrogenated with Raney-Ni in abs. alcohol at 19° until 2 moles of

H_2 are absorbed → 1-(4,5-dimethoxybenzoyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline. Y: 78%. F. e. s. E. Schlittler and A. Lindemann, Helv. *32*, 1880 (1949); in the presence of a base s. J. A. Barltrop and D. A. H. Taylor, Soc. *1951*, 108; with PtO_2 s. D. R. Howton and D. R. V. Golding, J. Org. Chem. *15*, 1 (1950).

Nickel/alkalis

Carboxylic acids from ethylenecarboxylic acids C : C → CHCH

s. *2*, 74; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, Am. Soc. *72*, 3539 (1950)

Palladium-carbon *Pd-C*

Selective hydrogenation

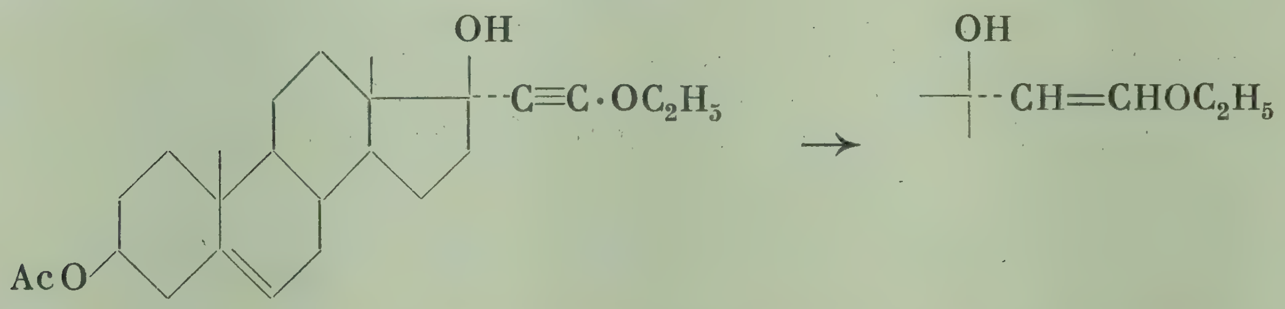
s. *4*, 81; 5, 56; s. a. H. Moreu et al., Bl. *1949*, 475

Palladium-calcium carbonate/pyridine *Pd-$CaCO_3/C_5H_5N$*

Selective and partial hydrogenation

Ethylene from acetylene derivatives C⋮C → CH : CH

92.

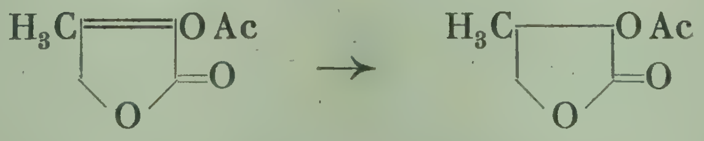


A soln. of 300 mg. 3β-acetoxy-17β-hydroxy-17α-ethoxyethynyl-Δ^5-androstene in pyridine shaken under H_2 with 2.5%-Pd-$CaCO_3$ for ca. 17 min. until the calculated amount of H_2 is absorbed → 250 mg. 3β-acetoxy-17β-hydroxy-17α-ethoxyvinyl-Δ^5-androstene. H. Heusser, K. Eichenberger, and P. A. Plattner, Helv. *33*, 370 (1950); s. a. C. Djerassi, R. Yashin, and G. Rosenkranz, Am. Soc. *72*, 5750 (1950).

Palladium hydroxide-calcium carbonate *$Pd(OH)_2$-$CaCO_3$*

Hydrogenation of enolacetates C : C(OAc) → CHCH(OAc)

93.

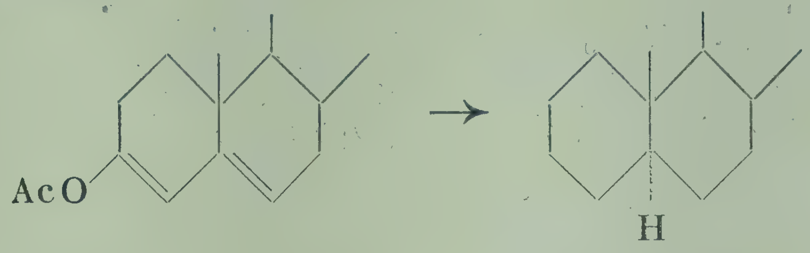


$\Delta^{\alpha,\beta}$-α-Acetoxy-β-methylbutenolide hydrogenated in alcohol with 2%-$Pd(OH)_2$-$CaCO_3$ for 1 hr. after reduction of the catalyst → α-acetoxy-β-methylbutanolide. Y: ca. 100%. F. e. s. F. Fleck et al., Helv. *33*, 130 (1949).

Platinum oxide *PtO_2*

Hydrocarbons from enolesters trans-Hydrogenation ←

94.



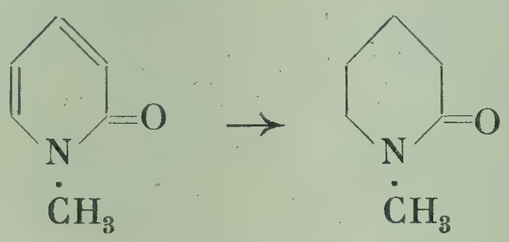
Cholestenone enol acetate hydrogenated with prehydrogenated PtO_2 in alcohol → cholestane. Y: 90%. F. e. s. H. H. Inhoffen et al., A. *568,* 52 (1950).

Hydrogenation of N-heterocyclic rings ←

s. *4,* 86; s. a. G. R. Clemo et al., Soc. *1950,* 1140

Piperidones from pyridones

95.



1-Methyl-2-pyridone hydrogenated 17 hrs. with PtO_2 in glacial acetic acid at 2-3.5 atm. and 26° → 1-methyl-2-piperidone. Y: 87.5%. N. J. Leonard and E. Barthel, Jr., Am. Soc. *71,* 3098 (1949); with Raney-Ni s. J. A. Gautier and J. Renault, R. *69,* 421 (1950).

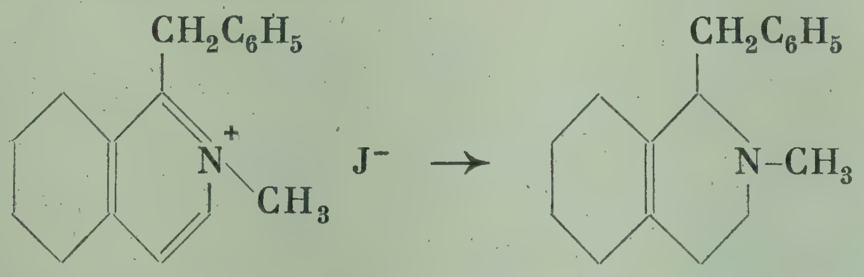
Selective hydrogenation of cyclic quaternary ammonium salts

s. *6,* 91

Platinum oxide/sodium hydroxide/iodine *$PtO_2/NaOH/I$*

Partial hydrogenation of cyclic quaternary ammonium salts

96.

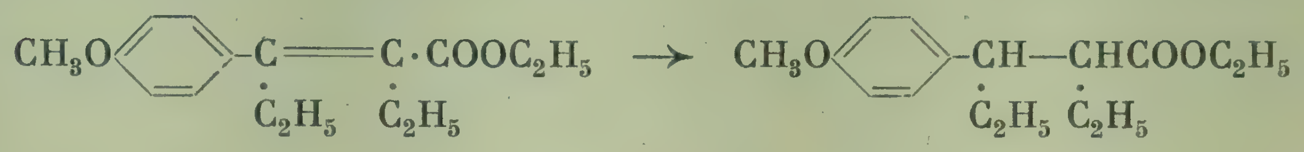


1-Benzyl-5,6,7,8-tetrahydroisoquinoline methiodide in aq.-methanolic NaOH hydrogenated ca. 2 hrs. with Adams catalyst (PtO_2) in the presence of a little iodine → 2-methyl-1-benzyl-1,2,3,4,5,6,7,8-octahydroquinoline (isolated as picrate). Y: 82%. F. e. s. R. Grewe, A. Mondon, and E. Nolte, A. *564,* 161 (1949).

Platinum oxide/palladium *PtO_2/Pd*

Hydrogenation of ethylene derivatives C:C → CHCH

97.



Ethyl (α,β-diethyl-p-methoxy)cinnamate in ethanol hydrogenated with PtO_2 and Pd black in a Parr hydrogenator at 60 lbs./sq. in. until the H_2-uptake is complete in ca. 4 hrs. → ethyl (2-ethyl-3-anisyl)valerate. Y: 97%. A. J. Shukis and J. J. Ritter, Am. Soc. *72*, 1488 (1950).

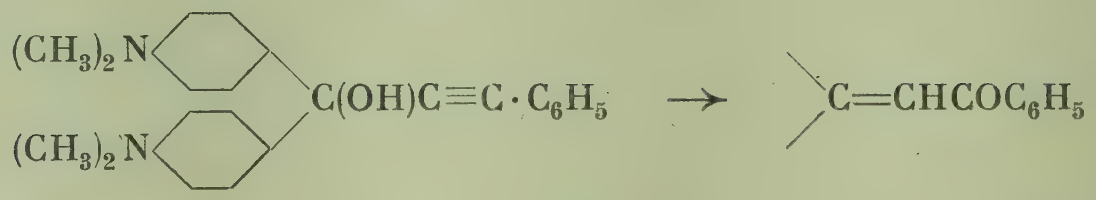
Rearrangement

Hydrogen/Oxygen Type HC↶HO

Sulfuric acid *H_2SO_4*

α,β-Ethyleneketones from α,β-acetylenealcohols ←

98.



Bis-(p-dimethylaminophenyl)(phenylethynyl)carbinol refluxed 10 min. in alc. H_2SO_4 → 1,1-bis-(p-dimethylaminophenyl)-3-phenyl-1-propen-3-one. Y: 90%. C. Dufraisse, J. Lefrancq, and P. Barbieri, R. *69*, 380 (1950).

Exchange

Oxygen ↑ HC⇅O

Sodium *Na*

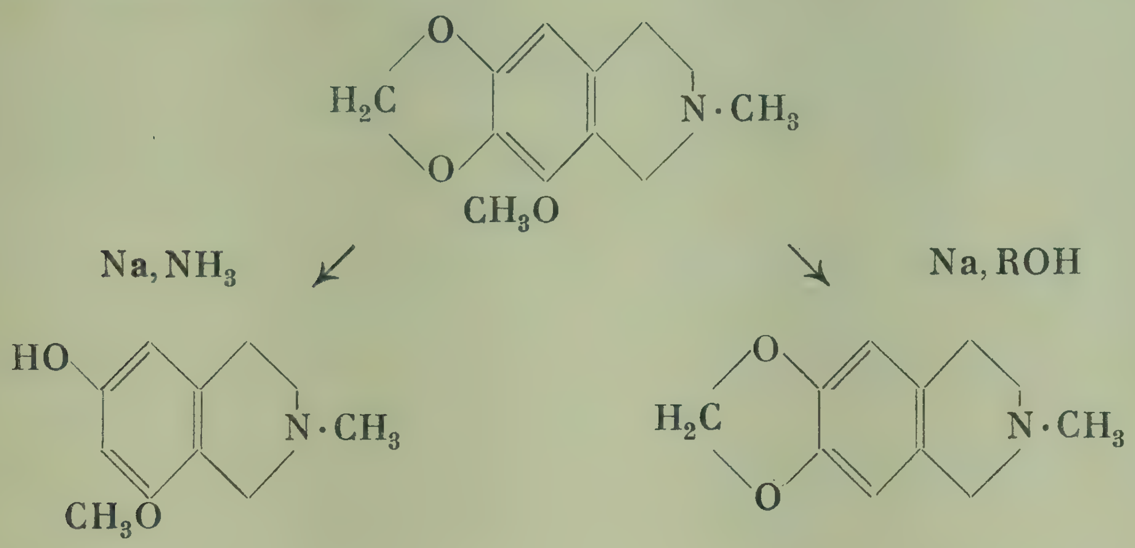
β-Hydroxyketones from β-ketocarboxylic acid esters ←

s. *6*, 216

Sodium and sodium/liq. ammonia *Na and Na/NH_3*

Reductive cleavage of ethers ←

99.



Hydrocotarnine (prepn., s. 112)

dissolved in ether, added to liq. NH_3 containing NH_4Cl, then Na added cautiously with stirring until a permanent blue color is obtained → 6-hydroxy-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline. Y: 96 %.

and 6 atoms Na in xylene boiled with vigorous stirring until the Na was finely dispersed, then isoamyl alcohol run in, and stirring continued for 20 min. after the first vigorous reaction has subsided → hydrohydrastinine Y: 60%.

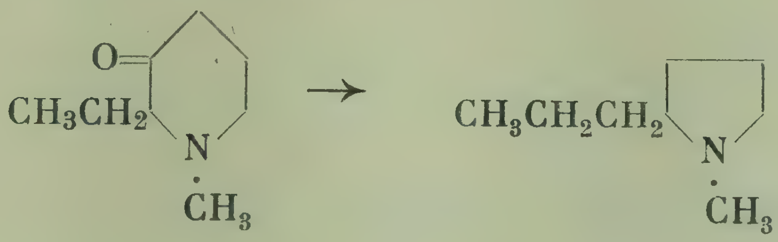
D. B. Clayson, Soc. *1949*, 2016.

Zinc and stannous chloride s. Stannous chloride and zinc *Zn/$SnCl_2$*

Zinc amalgam *Zn,Hg*

Amines from α-aminoketones with rearrangement
Clemmensen reduction
Ring contraction and enlargement ←

100.



A soln. of 1-methyl-2-ethyl-3-piperidone in concd. HCl added cautiously to Zn-amalgam, after the vigorous reaction has subsided refluxed 12 hrs. with repeated additions of concd. HCl → 1-methyl-2-n-propylpyrrolidine. Y: 65-71%. F. e. s. N. J. Leonard et al., Am. Soc. *71*, 3094, 3098, 3100 (1949); *72*, 3632 (1950); ring enlargement s. G. R. Clemo and H. Vipond, Chemistry and Industry *1949*, 856.

Lithium boron hydride $LiBH_4$

Lactones from ketocarboxylic acids ○
s. *6*, 53

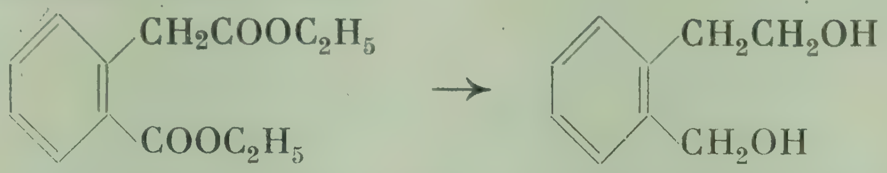
Lithium aluminum hydride $LiAlH_4$

Hydrocarbons from sulfonic acid esters $ROSO_2R' \rightarrow RH$
s. *6*, 47

Alcohols from carboxylic acids and esters ←
s. *3*, 52; *5*, 60; s. a. S. P. Ligthelm, E. v. Rudloff, and D. A. Sutton, Soc. *1950*, 3187

from carboxylic acid esters $COOR \rightarrow CH_2OH$

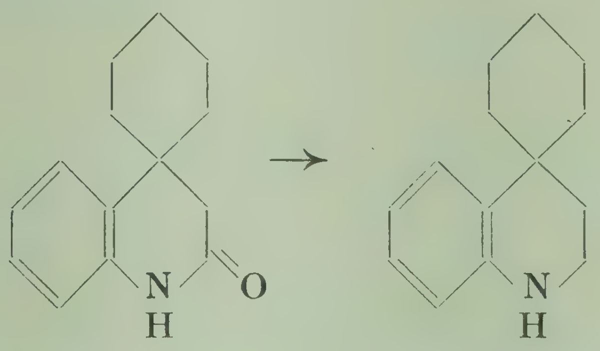
101.



A soln. of ethyl homophthalate in dry ether added to ethereal $LiAlH_4$ at such a rate that gentle refluxing is maintained, and allowed to stand overnight → o-2-hydroxyethylbenzyl alcohol. Y: 91%. E. L. Anderson and F. G. Holliman, Soc. *1950*, 1037; steroids s. D. Magrath et al., Soc. *1950*, 2393.

Cyclic amines from lactams ←

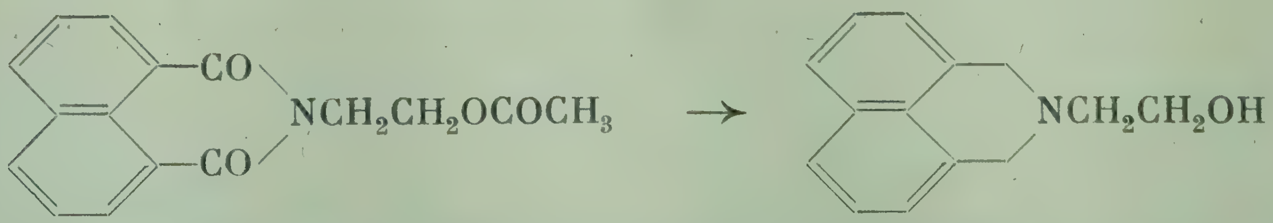
102.



Spiro(cyclohexane-1,4′-dihydrocarbostyril) in dry benzene added dropwise over 1 hr. to a soln. of 100% excess $LiAlH_4$ in ether, which is then distilled off, finally refluxed 24 hrs. → spiro(cyclohexane-1,4′-1′,2′,3′,4′-tetrahydroquinoline). Y: 96%. L. H. Schwartzman, J. Org. Chem. *15*, 517 (1950); s. a. O. E. Edwards and L. Marion, Am. Soc. *71*, 1694 (1949); R. B. Moffett, J. Org. Chem. 14, 862 (1949); indoles from oxindoles s. P. L. Julian and A. Magnani, Am. Soc. *71*, 2307 (1949).

Pyridine ring from dicarboxylic acid imides

103.

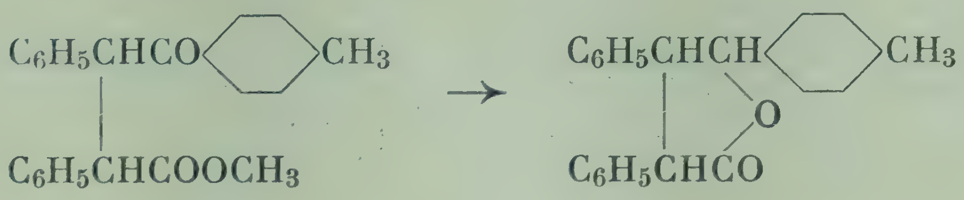


Anhydrous ether and $LiAlH_4$ stirred and refluxed for 2 hrs., then the condenser replaced by a Soxhlet extraction apparatus with N-(β-acetoxyethyl)naphthalimide in the extraction thimble, and refluxing continued for 20 hrs. → 2,3-dihydro-1-benz[de]isoquinoline-2-ethanol. Y: 68.5%. W. L. Garbrecht, J. H. Hunter, and J. B. Wright, Am. Soc. *72*, 1359 (1950); s. a. R. B. Moffett, J. Org. Chem. *14*, 862 (1949).

Aluminum alkoxide *Al(OR)$_3$*

Lactones from ketocarboxylic acid esters ○

104.

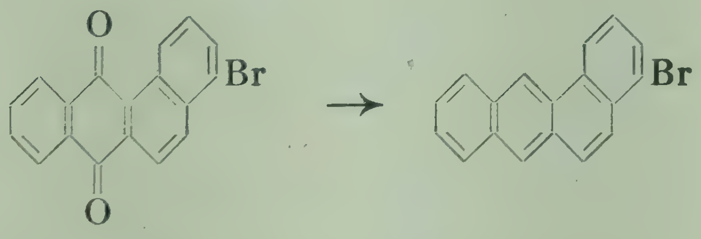


Methyl α,β-diphenyl-β-p-toluylpropionate heated with Al-isopropoxide and isopropanol → α,β-diphenyl-γ-p-tolyl-γ-butyrolactone. Y: 82%. J. A. McRae, R. A. B. Bannard, and R. B. Ross, Can. J. Research *28 B*, 73 (1950); s. a. J. English, Jr., and J. E. Dayan, Am. Soc. *72*, 4187 (1950); method s. F. Bergmann, H. E. Eschinazi, and D. Schapiro, Am. Soc. *64*, 557 (1942).

Stannous chloride and zinc *SnCl$_2$ and Zn*

Anthracenes from anthraquinones ←

105.

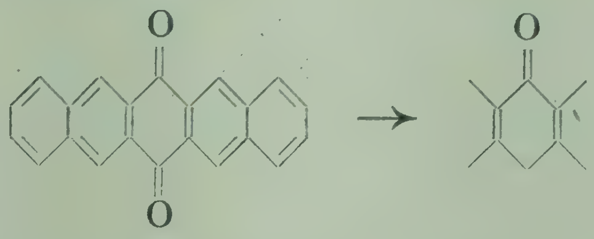


1.5 gm. 4′-bromo-1,2-benzanthraquinone refluxed 1 hr. with $SnCl_2$ in acetic acid-concd. HCl, and the crude product reduced further by boiling with Zn-dust in 2 *N* NaOH for 3 hrs. → 1.4 gm. 4′-bromo-1,2-benzanthracene. F. e. s. G. M. Badger and A. R. M. Gibb, Soc. *1949*, 799.

Hyposulfite $S_2O_4^{--}$

Anthrones from anthraquinones CO → CH_2

106.



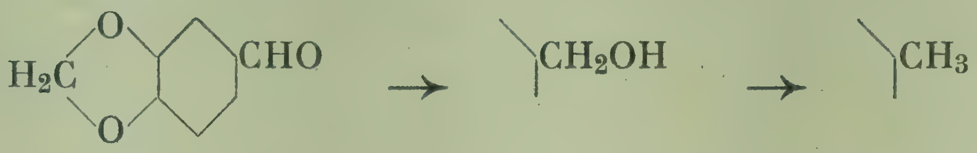
7 gm. pentacene-6,13-quinone, NaOH, and $Na_2S_2O_4$ in water heated almost to boiling for 1 hr. with exclusion of air → 6 gm. 6-pentacenone. E. Clar, B. *82*, 495 (1949).

Copper chromite *$CuCr_2O_4$*

Hydrocarbons from aldehydes via prim. alcohols

$CHO \rightarrow CH_2OH \rightarrow CH_3$

107.



Piperonal hydrogenated in dioxane with $CuCr_2O_4$ at 300 atm. and 160-175° for 1¼ hrs. → piperonyl alcohol (Y: 98%) hydrogenated with $CuCr_2O_4$ at 375 atm. and 280° for 2 hrs. → 3,4-methylenedioxytoluene (Y: 84.5%). W. Reeve and J. D. Sterling, Jr., Am. Soc. *71*, 3657 (1949).

Hydrocarbons from ketones

$CO \rightarrow CH_2$

s. *4*, 97; carboxylic acids from ketocarboxylic acids s. F. C. Novello and M. E. Christy, Am. Soc. *73*, 1267 (1951)

Alcohols and hydrocarbons from oxo compounds

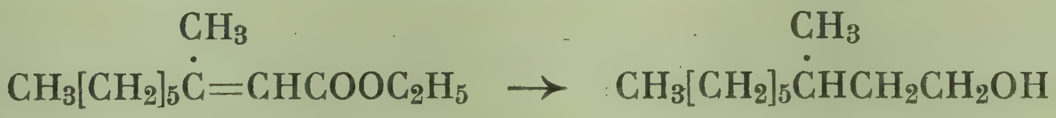
←

108. Ar. ketones and methoxy ar. aldehydes may be hydrogenated over $CuCr_2O_4$ at an initial H_2-pressure of 220-340 atm. to the corresponding carbinol at 110-130° or the alkylbenzene or cresol at 185-250° in nearly 100% yields.—The o- and p-hydroxybenzaldehydes are reduced to o- and p-cresol at 110-130° with yields of 86 and 73% respectively, while m-hydroxybenzaldehyde gives a 84% yield of m-hydroxybenzyl alcohol at this temp.—Both o- and p-hydroxyketones are reduced to alkylphenols at 110-130° with yields of 75-90%. E. s. D. Nightingale and H. D. Radford, J. Org. Chem. *14*, 1089 (1949).

Alcohols from ethylenecarboxylic acid esters

←

109.



$$CH_3[CH_2]_5\overset{CH_3}{\dot{C}}{=}CHCOOC_2H_5 \longrightarrow CH_3[CH_2]_5\overset{CH_3}{\dot{C}}HCH_2CH_2OH$$

Ethyl 3-methylnonenoate hydrogenated with $CuCr_2O_4$ at 250° and an initial maximum pressure of 3490 p. s. i./20° for 7 hrs. → 3-methyl-1-nonanol. Y: 86%. J. Cason et al., J. Org. Chem. *15*, 135 (1950).

Nickel *Ni*

Hydrocarbons from sulfonic acid esters

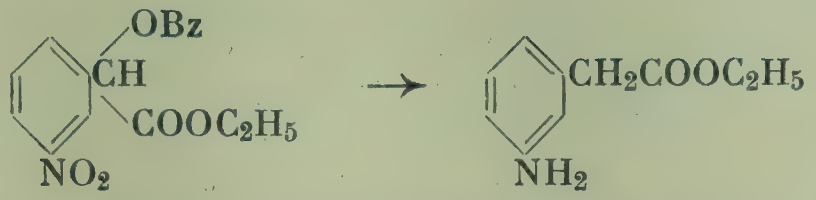
ArOTs → ArH

s. *6*, 9

Nickel/sodium carbonate Ni/Na_2CO_3

Carboxylic acid esters from α-acoxycarboxylic acid esters, simultaneously: amines from nitro compounds ←

110.

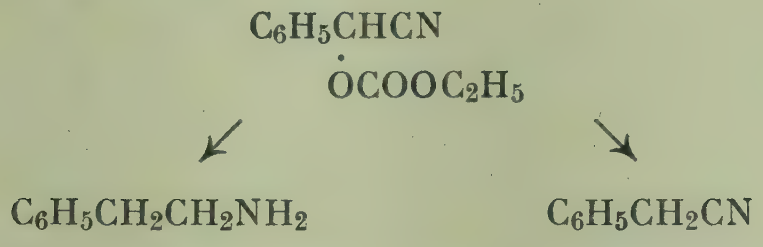


A suspension of ethyl m-nitro-O-benzoylmandelate (prepn. s. 239), Na-carbonate, and Raney-Ni in abs. alcohol hydrogenated at 150-200 atm. and, during the last 50 min., at 120-130° → ethyl m-aminophenylacetate. Y: 87%. M. W. Cronyn, J. Org. Chem. *14*, 1013 (1949).

Palladium-carbon *Pd-C*

Amines and nitriles from cyanocarbonates
Directing the hydrogenation by acids ←

111.



$$\begin{tikzcd} & \underset{OCOOC_2H_5}{C_6H_5\dot{C}HCN} \arrow[dl] \arrow[dr] & \\ C_6H_5CH_2CH_2NH_2 & & C_6H_5CH_2CN \end{tikzcd}$$

O-Carbethoxymandelonitrile hydrogenated

with Pd-C in methanol-concd. H_2SO_4 at 2 atm. and room temp. → β-phenylethylamine. Y: 92%.

ca. 4 hrs. in benzene with Pd-black in a H_2-stream to remove the CO_2 formed → benzyl cyanide. Y. 90%

K. Kindler and K. Schrader, A. *564*, 49 (1949).

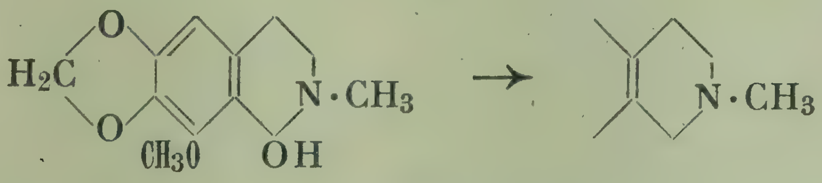
Oximes from α-nitroethylene derivatives $CH{:}CHNO_2 \rightarrow CH_2CH{:}NOH$

s. *5*, 65; s. a. B. Reichert and H. Marquardt, Pharmazie *5*, 10 (1950)

Platinum oxide *PtO*$_2$

Replacement of hydroxyl by hydrogen OH → H

112.



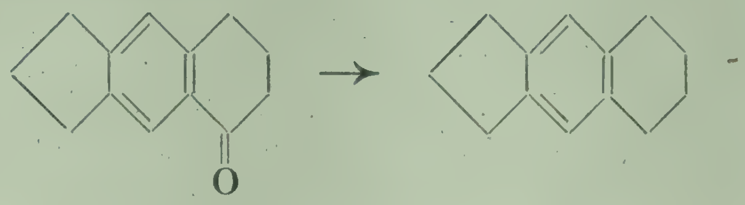
Cotarnine hydrochloride hydrogenated in water with PtO_2 (Adams') catalyst at room temp. and 2 atm. until the theoretical amount of H_2 has been absorbed after 60-90 min. → hydrocotarnine (startg. m. f. 99). Y: 95%. D. B. Clayson, Soc. *1949*, 2016.

Hydrocarbons from enolesters ←

s. *6*, 94

Hydrocarbons from ketones $CO \rightarrow CH_2$

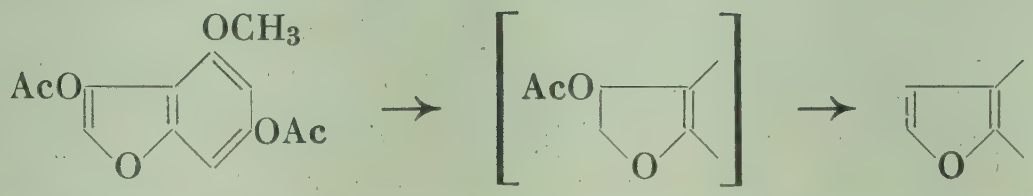
113.



1-Keto-1,2,3,4-tetrahydro-6,7-cyclopentenonaphthalene in glacial acetic acid-concd. HCl shaken with PtO_2 (Adams' catalyst) in a H_2 atmosphere for 40 hrs. until the absorption of H_2 ceases → 1,2,3,4-tetrahydro-6,7-cyclopentenonaphthalene. Y: 94%. P. A. Plattner, A. Fürst, and W. Keller, Helv. *32*, 2464 (1949).

Ethylene derivatives from enol acetates $C{:}C(OAc) \rightarrow C{:}CH$

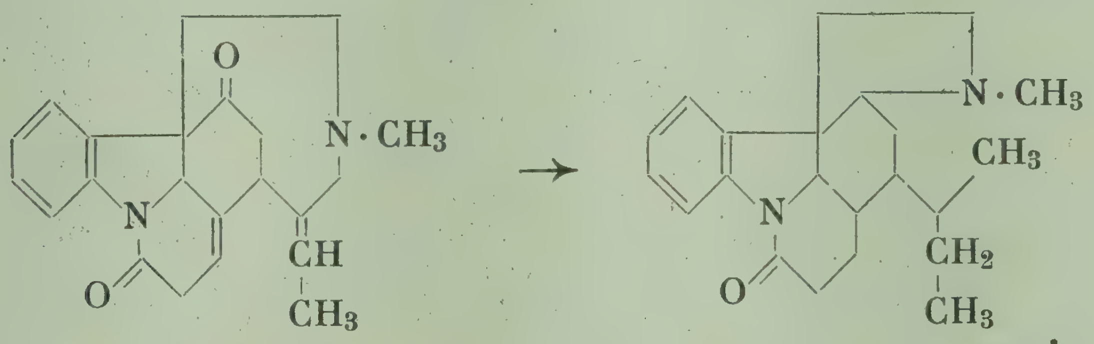
114.



3,6-Diacetoxy-4-methoxycoumarone hydrogenated with PtO_2 in glacial acetic acid until, after 22 min., the theoretical quantity of H_2 has been absorbed, filtered, and acetic acid split off by distillation in vacuo → 4-methoxy-6-acetoxycoumarone. Y: 91%. F. e. s. W. Gruber and K. Horváth, M. *80*, 563 (1949).

Reductive ring contraction ←

115.



Desoxy-N-methylisopseudostrychnine hydrogenated in 0.25 *N* acetic acid with PtO_2 at room temp. for 4 hrs. → desoxy-N-methylhexahydrochano-isostrychnine. Y: 65%. F. e. s. H.-G. Boit, B. *83*, 217 (1950).

Via intermediates *v.i.*

Hydrocarbons from oxo compounds via hydrazones according to Wolff-Kishner $CO \rightarrow CH_2$

Simplified procedures

s. *2*, 96; s. a. Oesterr. Chem.-Ztg. *50*, 5 (1949)

Huang-Minlon modification

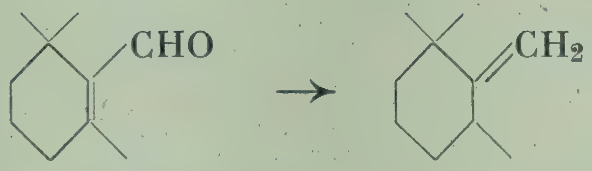
s. *3*, 57; s. a. Ng. Ph. Buu-Hoï and Ng. Hoán, Am. Soc. *73*, 98 (1951); W. E. Bachmann and E. J. Fornefeld, Am. Soc. *73*, 51 (1951)

116. In the case of steroids the reduction of the keto groups proceeds normally at positions C_3, C_7, C_{12}, C_{17} and C_{20}, but the C_{11}-keto group remains unattacked. Huang-Minlon, Am. Soc. *71*, 3301 (1949).

steric hindrance s. J. Cason, G. Sumrell, and R. S. Mitchell, J. Org. Chem. *15*, 850 (1950)

Wolff-Kishner reduction with migration of a carbon carbon double bond

117.



In the Wolff-Kishner reduction of α,β-ethyleneoxo compounds, migration of the double bond can occur, permitting synthesis of compounds not otherwise available, e.g. compounds with a semicyclic methylene group.—E: 3 gm. β-cyclocitral allowed to stand at room temp. for 1 hr. with hydrazine hydrate in alcohol, refluxed 30 min., a soln. of Na in abs. alcohol added, and heated at 200-210° in a sealed tube overnight → 2.28 gm. 1,1,3-trimethyl-2-methylenecyclohexane. F. e. s. G. Lardelli and O. Jeger, Helv. *32*, 1817 (1949).

Nitrogen ↑ HC↓↑N

Sodium carbonate *Na_2CO_3*

Hydrocarbons from sulfonic acid hydrazides $NHNHSO_2R \rightarrow H$

s. *6*, 121

Sodium nitrite *$NaNO_2$*

Replacement of amino groups by hydrogen $NH_2 \rightarrow H$

s. *2*, 103; s. a. R. B. Carlin and W. O. Forshey, Jr.. Am. Soc. *72*, 793 (1950)

Sulfuric acid *H_2SO_4*

Aldehydes from 1-acyl-1,2-dihydroquinaldonitriles (Reissert compounds)

s. *6*, 122

Copper chromite *$CuCr_2O_4$*

Hydrocarbons from tert. amines $NR_2 \rightarrow H$
Hydrogenolysis of Mannich bases
s. *6*, 730

Hydriodic acid *HI*

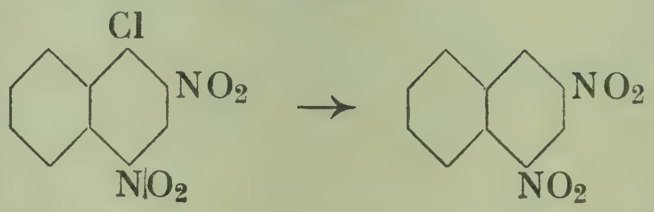
Methyl ketones from α-diazoketones $COCHN_2 \rightarrow COCH_3$
s. *3*, 60; s. a. R. B. Wagner and J. M. Tone, Am. Soc. *72*, 3477 (1950)

Halogen ↑ HC⇅Hal

Copper *Cu*

Replacement of chlorine by hydrogen $Cl \rightarrow H$

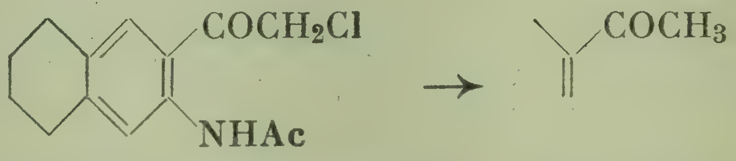
118.



Ar. nitrochloro compounds containing a nitro group ortho to the chlorine undergo dechlorination when heated with Cu-powder and an organic acid at 150-200°.—E: Cu-powder added in several portions over a period of 5 min. at 150-200° to a manually stirred mixture of benzoic acid and 1-chloro-2,4-dinitronaphthalene → 1,3-dinitronaphthalene. Y: 74%. F. e. s. W. T. Smith, Jr., Am. Soc. *71*, 2855 (1949).

Zinc *Zn*

119.



10 gm. 6-acetamido-7-chloroacetyltetralin, Zn (etched with dil. H_2SO_4 and washed with water), and alcohol refluxed with vigorous stirring for 8 hrs. → 8.42 gm. 6-acetamido-7-acetyltetralin. F. e. s. K. Schofield, T. Swain, and R. S. Theobald, Soc. *1949*, 2399.

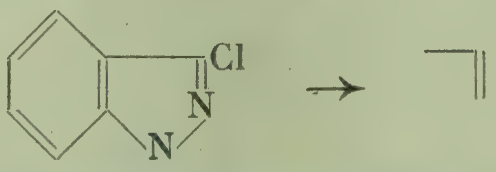
Stannous chloride *$SnCl_2$*

Methyl ketones from α-bromoketones $Br \rightarrow H$
s. *3*, 63; s. a. J. Siegle and B. E. Christensen, Am. Soc. *72*, 4186 (1950)

Phosphorus/hydriodic acid *P/HI*

Replacement of chlorine by hydrogen $Cl \rightarrow H$

120.



3-Chloroindazole, red P, and constant-boiling HI (d. 1.7) refluxed 24 hrs. → indazole. Y: 82-86%. E. F. M. Stephenson, Org. Synth. *29*, 54 (1949); s. a. W. R. Boon, W. G. M. Jones, and G. R. Ramage, Soc. *1951*, 96.

Chromous chloride *CrCl$_2$*

Replacement of halogen by hydrogen Hal → H
s. *4*, 112; s. a. Am. Soc. *72*, 4077, 4081 (1950)

Palladium-barium sulfate *Pd-BaSO$_4$*

simultaneously:
amines from nitro compounds
s. *6*, 35

Aldehydes from carboxylic acid chlorides COCl → CHO
s. *1*, 99, 101; s. a. W. K. Detweiler and E. D. Amstutz, Am. Soc. *72*, 2882 (1950); H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. *73*, 1414 (1951)

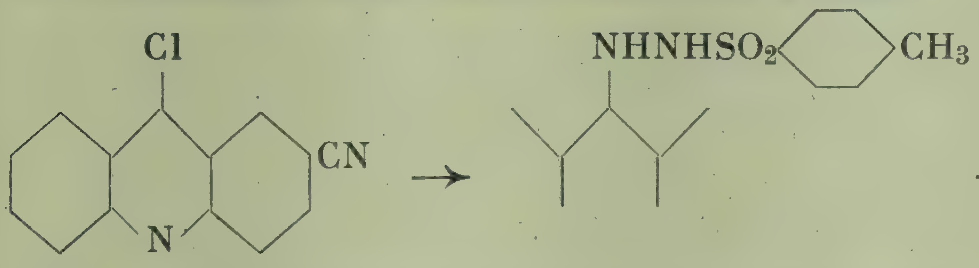
Palladium-carbon *Pd-C*

Replacement of halogen by hydrogen Hal → H
s. *6*, 731

Via intermediates *v.i.*

Replacement of active chlorine by hydrogen via sulfonic acid hydrazides in compounds with easily reducible groups Cl → H

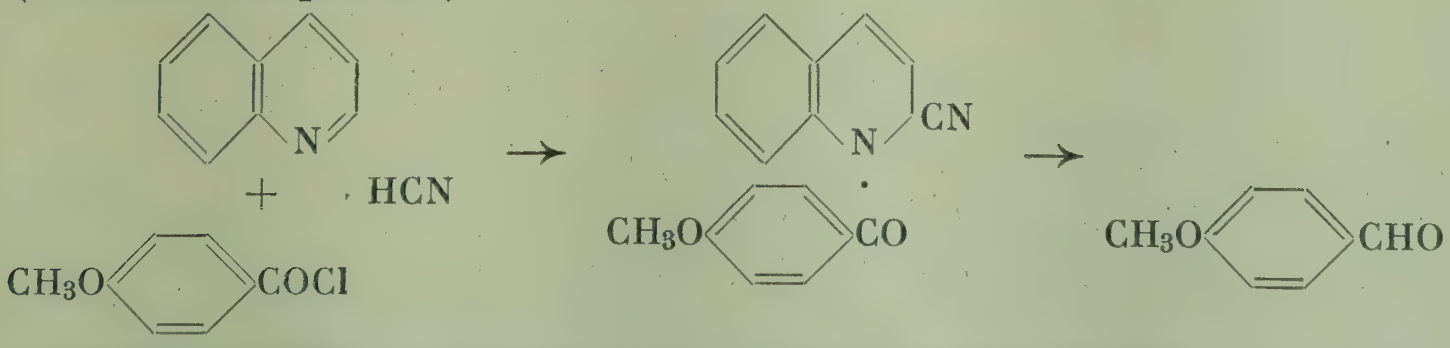
121.



Cold satd. chloroform solutions of p-toluenesulfonylhydrazide and 9-chloro-2-cyanoacridine mixed, and set aside for 1-2 days → crude 9-[N′-(p-toluenesulfonyl)hydrazino]-2-cyanoacridine hydrochloride (Y: ca. 100%) decomposed with Na$_2$CO$_3$ → 2-cyanoacridine (Y: 65%). —In other cases the hydrazides were prepared in the presence of dry HCl, and decomposed with NaOH. F. e. s. A. Albert and R. Royer, Soc. *1949*, 1148.

Aldehydes from carboxylic acid chlorides via 1-acyl-1,2-dihydroquinaldonitriles (Reissert compounds) COCl → CHO

22.



Anhydrous HCN poured at about —5° into freshly distilled quinoline, under further cooling a soln. of 4-methoxybenzoyl chloride in abs.

benzene dropped in over a period of 10 min., and allowed to stand at room temp. for ca. 16 hrs. → 1-(p-methoxybenzoyl)-1,2-dihydroquinaldonitrile (Y: 88%) steam-distilled with 10 N H_2SO_4 → p-methoxybenzaldehyde (Y: 98%). F. e., also without isolation of the intermediate, s. J. M. Grosheintz and H. O. L. Fischer, Am. Soc. *63*, 2021 (1941).

Sulfur ↑ HC ⇅ S

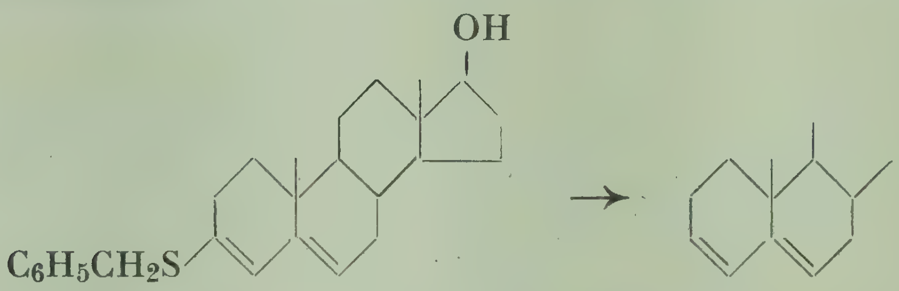
Nickel *Ni*

Replacement of sulfhydryl by hydrogen SH → H
Imidazoles from 2-mercaptoimidazoles

s. *5*, 77; s. a. R. A. Turner, Am. Soc. *71*, 3476 (1949)

Desulfuration of thioenolethers C:C(SR) → C:CH
Deactivated catalyst

123.



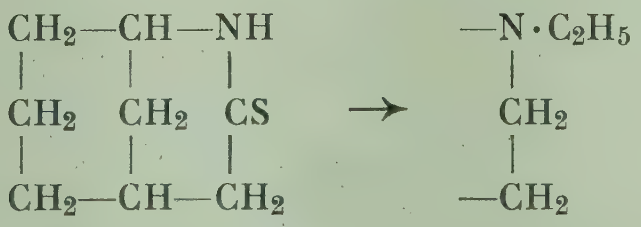
Benzyl enethiolether from testosterone refluxed 4 hrs. in acetone with Raney-Ni, which has been partially deactivated by refluxing 1 hr. in acetone (cf. Synth. Meth. 4, 118) → $\Delta^{3,5}$-androstadien-17β-ol. Y: 87%. —If the catalyst is not deactivated, the double bonds are hydrogenated. F. e. s. G. Rosenkranz, S. Kaufmann, and J. Romo, Am. Soc. *71*, 3689 (1949).

Hydrocarbons from mercaptals $C(SR)_2 \rightarrow CH_2$

s. *3*, 72; carbohydrates s. M. L. Wolfrom et al., Am. Soc. *71*, 4057 (1949); *73*, 1528 (1951).

Amines from carboxylic acid thioamides $CSN\langle \rightarrow CH_2N\langle$
Cyclic amines from thiolactams
N-Alkylation

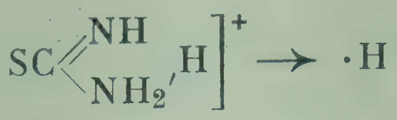
124.



$$\begin{array}{ccccc} CH_2-CH-NH & & & & -N\cdot C_2H_5 \\ | \quad\ \ | \quad\ \ | & & & & | \\ CH_2 \quad CH_2 \quad CS & & \rightarrow & & CH_2 \\ | \quad\ \ | \quad\ \ | & & & & | \\ CH_2-CH-CH_2 & & & & -CH_2 \end{array}$$

A soln. of *cis*-3-aminocyclohexaneacetic acid thiolactam (prepn. s. 636) in abs. ethanol, protected with a soda-lime tube, refluxed for 3 hrs. with Raney-Ni → 2 ethyl-2-azabicyclo[3.3.1]nonane. Y: 76%. Also without alkylation s. M. W. Cronyn, J. Org. Chem. *14*, 1013 (1949); noncyclic amines s. E. C. Kornfeld, J. Org. Chem. *16*, 131 (1951).

Hydrocarbons from thiouronium salts



$\left[SC\begin{matrix}NH\\NH_2\end{matrix}H\right]^+ \rightarrow \cdot H$

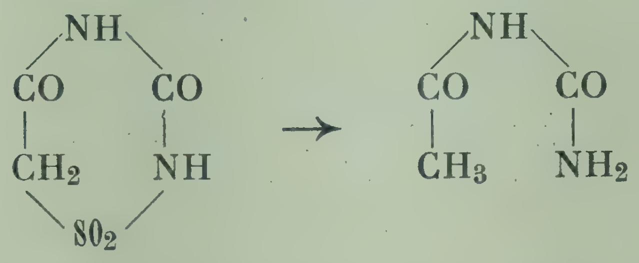
s. *2,* 111; s. a. G. M. Badger et al., Soc. *1950,* 2326

Thiophene ring opening C

s. *5,* 79; s. a. Am. Soc. *71,* 4010 (1949); E. J. Modest and J. Szmuszkowicz, Am. Soc. *72,* 577 (1950)

1,2,4-Thiadiazine ring opening

125.



Trimethylene-1,2,4-thiadiazine-3,5-dione-1,1-dioxide refluxed 4 hrs. with Raney-Ni according to Mozingo in 75%-ethanol → acetylurea. Y: 79%. F. e. s. P. N. Rylander and E. Campaigne, J. Org. Chem. *15,* 249 (1950).

Nickel/sodium carbonate *Ni/Na_2CO_3*

Hydrocarbons from thioethers
Carboxymethyl thioethers as intermediates SR → H

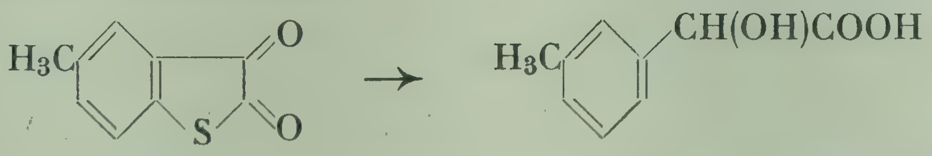
s. *6,* 482

Nickel/aluminum *Ni/Al*

Reductions of sulfur compounds with nickel aluminum alloy ←

Thianaphthene ring opening

126.



In general, this reaction proceeds smoothly, and good yields of desulfurized products are obtained.—E: 15 gm. 5-methylthianaphthenequinone (prepn. s. 818) in 10%-NaOH reacted with Ni, Al-alloy → 9.8 gm. m-methylmandelic acid. F. e. s. D. Papa, E. Schwenk, and H. F. Ginsberg, J. Org. Chem. *14,* 723 (1949).

Carbon ↑ HC⇅C

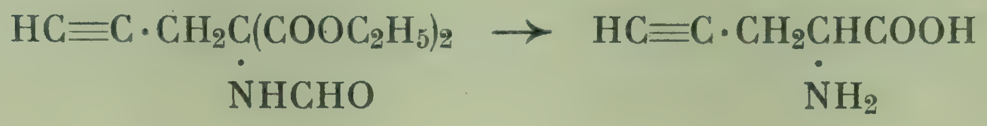
Sodium hydroxide *NaOH*

Subst. glutaric acids from arylmethylene-bis-acetoacetates ←

s. *6,* 759

α-Aminocarboxylic acids from α-formamidomalonic esters ←

127.



$$HC{\equiv}C\cdot CH_2\underset{NHCHO}{C}(COOC_2H_5)_2 \rightarrow HC{\equiv}C\cdot CH_2\underset{NH_2}{C}HCOOH$$

Diethyl propargylformamidomalonate refluxed 4 hrs. with 8%-NaOH, diluted with water, passed first through a column of Duolite C-10H to remove the base, then through a column of Duolite A-2 to remove the formic acid produced → propargylglycine. Y: 88.5%. H. Gershon, J. S. Meek, and K. Dittmer, Am. Soc. *71*, 3573 (1949).

s. a. *6*, 789

Potassium hydroxide *KOH*

Replacement of C-acyl by hydrogen COR → H

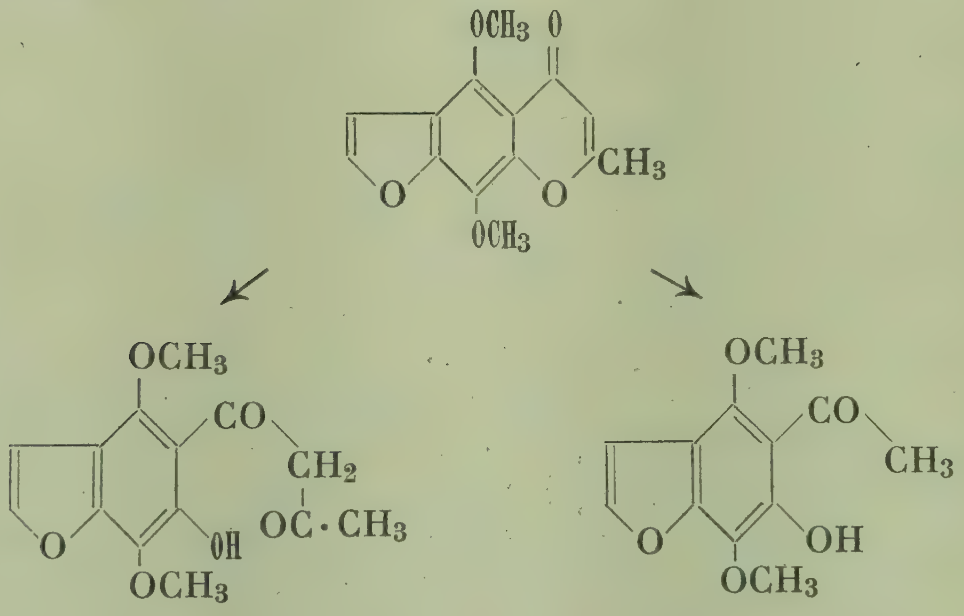
s. *5*, 80; s. a. P. J. Pollak and D. Y. Curtin, Am. Soc. *72*, 961 (1950)

Carboxylic acids from cyanocarboxylic acid esters ←

s. *6*, 700; s. a. K. Pettersson, Acta Chem. Scand. *4*, 395 (1950)

γ-Pyrone ring opening C

128.



A soln. of KOH in abs. alcohol at 70° poured onto 10 g. khellin, and shaken for 15 min. without further heating → 8.5 g. ω-acetokhellinone.

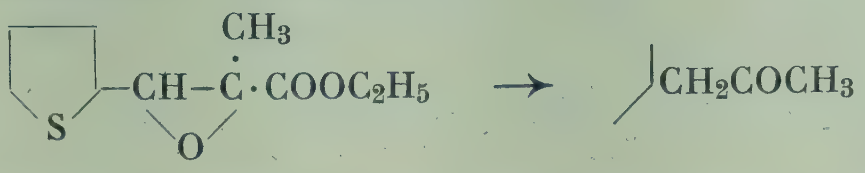
Khellin boiled with aq. KOH for 1 hr. → khellinone. Y: ca. 90%.

A. Schönberg and A. Sina, Am. Soc. *72*, 1611 (1950).

Sodium alkoxide *NaOR*

Ketones from glycidic acid esters ←

129.



Ethyl α-methyl-2-thiopheneglycidate refluxed with a slight excess of alc. NaOH, most of the alcohol evaporated, the Na-salt dissolved in water, acidified with HCl, extracted with ether, and the ether residue heated 5 min. at 120° → α-thienylacetone. Y: 87%. P. Cagniant, Bl. *1949*, 847.

β-Ketocarboxylic acid esters from β,β′-diketocarboxylic acid esters COR → H

s. *1*, 649, 770; *4*, 122; s. a. D. Libermann, J. Himbert, and L. Hengl, Bl. *1950*, 486

Sodium amide *$NaNH_2$*

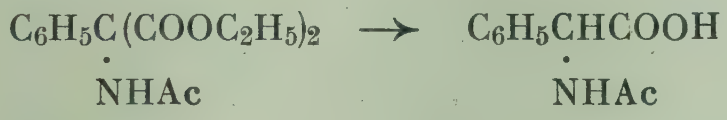
Replacement of cyano groups by hydrogen CN → H

s. *5*, 81; s. a. M. Jackman, F. C. Nachod, and S. Archer, Am. Soc. *72*, 716 (1950)

Sodium carbonate *Na_2CO_3*

α-Acetamidocarboxylic acids from acetamido-malonic esters and -α-cyanocarboxylic esters ←

130.



$$\underset{NHAc}{C_6H_5C(COOC_2H_5)_2} \rightarrow \underset{NHAc}{C_6H_5CHCOOH}$$

Alkylacetamidomalonic esters are refluxed overnight (ca. 16 hrs.) with an equal weight of Na-carbonate dissolved in 10 volumes of water. Alkylacetamidocyanoacetic esters are refluxed ca. 60 hrs. until evolution of NH_3 has practically ceased.—E: Benzylacetamidomalonic ester → acetyl-DL-phenylalanine. Y: 75%.—3-Indolemethyl-acetamidocyanoacetic ester → acetyl-DL-tryptophan. Y: 81%. F. e. s. N. F. Albertson, Am. Soc. *72*, 1396 (1950).

Sodium cyanide *NaCN*

Reverse Mannich reaction $CH_2N\langle \rightarrow H$

s. *5*, 82; cf. G. Zigeuner, M. *80*, 801 (1949)

Ammonia *NH_3*

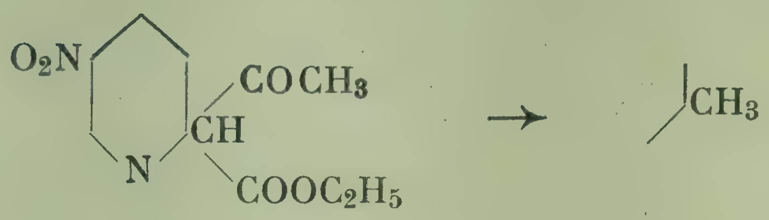
Carboxylic acids from barbituric acids C

s. *6*, 228

Sulfuric acid *H_2SO_4*

Hydrocarbons from β-ketocarboxylic acid esters ←

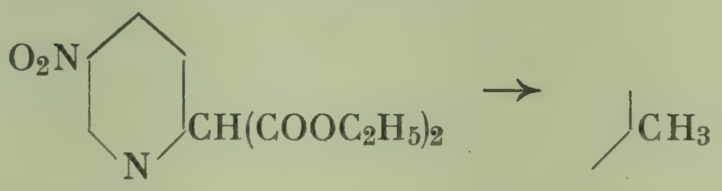
131.



Ethyl (5-nitro-2-pyridyl)acetoacetate heated in 10%-H_2SO_4 on a water bath for 5 hrs. → 2-methyl-5-nitropyridine. Y: 81%.—The methyl ketone could not be obtained. W. Gruber and K. Schlögl, M. *80*, 499 (1949).

Hydrocarbons from malonic acid esters ←

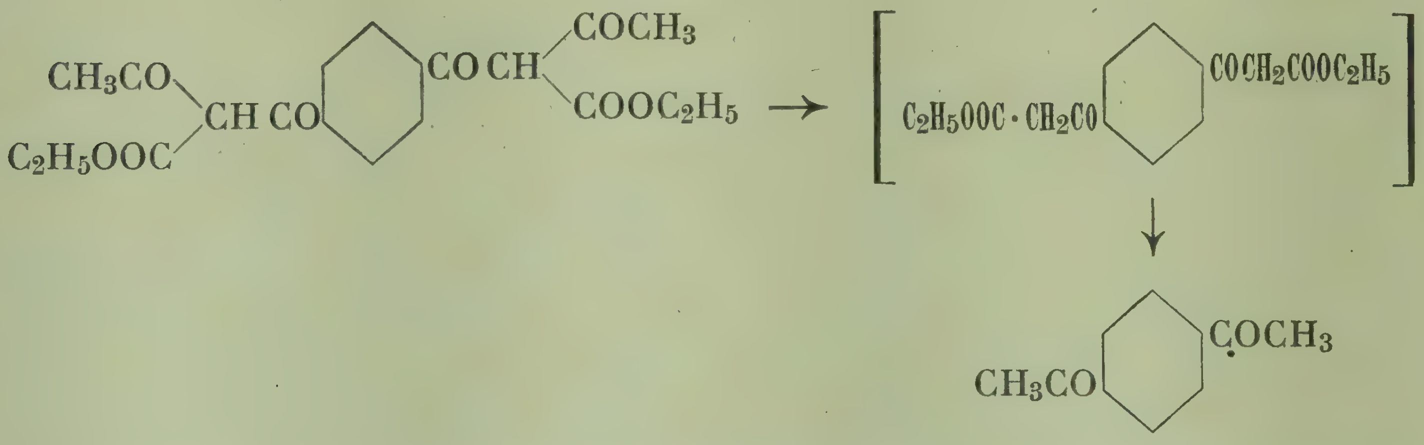
132.



(5-Nitro-2-pyridyl)malonic acid ester heated 4 hrs. at 120-130° with 1:2 H_2SO_4-water → 5-nitro-2-methylpyridine. Y: 90%. W. Gruber and K. Schlögl, M. *81*, 473 (1950).

Methyl ketones from β,β-diketocarboxylic acid esters ←

133.



Terephthaloyldiacetoacetic ester, alcohol, and concd. H_2SO_4 refluxed 14 hrs., water added, concentrated to its original volume, then refluxed for 8 hrs. more → p-diacetylbenzene. Y: 60%. Also isolation of the intermediates s. K. Schofield and R. S. Theobald, Soc. *1949*, 2404; method, see Kermack and Smith, Soc. *1929*, 814.

Methyl ketones from acylmalonic acid esters

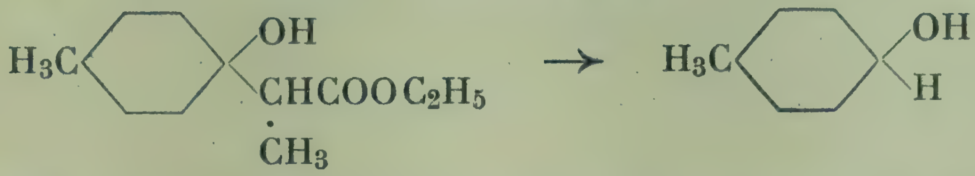
$COCH(COOC_2H_5)_2 \rightarrow COCH_3$

s. *6*, 285

Hydrochloric acid *HCl*

Hydrogenolysis of the carbon carbon bond ←

134.



A soln. of ethyl α-(4-methyl-1-hydroxycyclohexyl)propionate in dioxane hydrogenated with Cu-chromite at 270° and an initial pressure of 3400 lbs./sq. in./25° → 4-methylcyclohexanol. Y: 60-70%. R. L. Frank and R. E. Berry, Am. Soc. *72*, 2985 (1950); s. a. R. Connor and H. Adkins, Am. Soc. *54*, 4678 (1932).

Copper chromite *$CuCr_2O_4$*

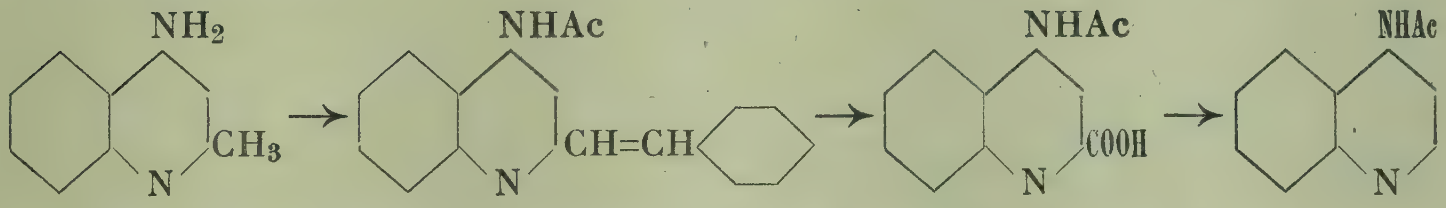
Dicarboxylic acids from dicyanocarboxylic acid esters ←

s. *6*, 705; s. a. E. C. Horning and A. F. Finelli, Org. Synth. *30*, 81 (1950)

Via intermediates *v.i.*

Replacement of methyl groups by hydrogen CH_3 → H
Styrylheterocyclics
Carboxylic acids from hydrocarbons
Decarboxylation

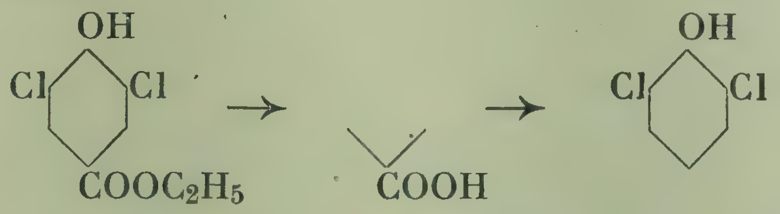
135.



4-Aminoquinaldine, benzaldehyde, and acetic anhydride heated 3 hrs. at 155-160° → 4-acetamido-2-styrylquinoline (Y: 91%) in pyridine-water treated at 18-20° with $KMnO_4$ during 1 hr., and stirring continued for 30 min. → 4-acetamidoquinaldinic acid (Y: 82%) added during 5 min. to paraffin at 290°, and worked up after a further 5 min. → 4-acetamidoquinoline (Y: 89%). F. e. s. R. Royer, Soc. *1949*, 1803.

Hydrocarbons from carboxylic acid esters via carboxylic acids COOR → H

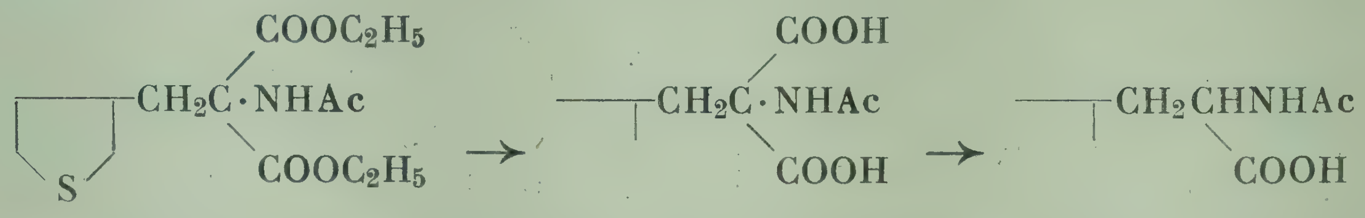
136.



Ethyl 3,5-dichloro-4-hydroxybenzoate hydrate (prepn. s. 572) heated 1 hr. on a steam bath with Claisen's alkali (KOH in methanol-water) → 3,5-dichloro-4-hydroxybenzoic acid (Y: 93-97%) heated slowly with dimethylaniline to 190-200°, then ca. 2 hrs. at this temp., until the evolution of gas has ceased → 2,6-dichlorophenol (Y: 80-91%). D. S. Tarbell, J. W. Wilson, and P. E. Fanta, Org. Synth. *29*, 35 (1949).

α-Acylaminocarboxylic acids from acylaminomalonic acid esters ←
Selective hydrolysis
Decarboxylation

137.



Diethyl 3-thenylacetamidomalonate and 10% NaOH mixed to a paste, let stand at room temp. for 24 hrs., or until soln. takes place, filtered, cooled in ice, and neutralized with 12 *N* HCl below 20° to prevent decarboxylation → 3-thenylacetamidomalonic acid (Y: 84%) boiled 2 hrs. with water, then evaporated to near dryness on a steam bath → N-acetyl-β-3-thienylalanine (Y: 84%).—The process can be performed in one step, but in this case no excess acid must be used to neutralize the alkali before boiling to prevent loss of the acid-labile thiophene derivative. R. G. Garst, E. Campaigne, and H. G. Day, J. Biol. Chem. *180*, 1013 (1949).

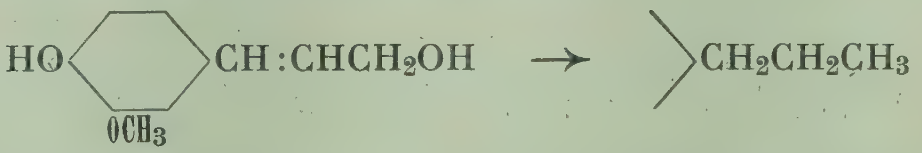
Elimination

Oxygen ↑ **HC ⇑ O**

Sodium/liq. ammonia *Na/NH₃*

Hydrocarbons from α,β-ethylenealcohols ←

138.

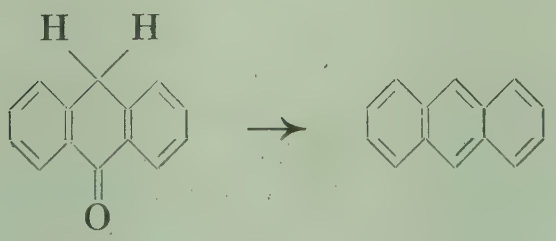


Na added to a soln. of coniferyl alcohol in liq. NH_3, and kept 5 days with Dry-Ice cooling → dihydroeugenol. Y: 86%. N. N. Shorygina, T. Y. Kefeli, and A. F. Semechkina, Ж. *19*, 1558 (1949); C. A. *44*, 3919 c.

Zinc/copper sulfate/alkali hydroxide ←

Anthracenes from anthrones ←

139.



2 *N* NaOH, toluene, and anthrone added to Zn-dust activated with aq. $CuSO_4$, and refluxed 12 hrs. → anthracene. Y: 93%. E. L. Martin, Am. Soc. *58*, 1438 (1936); with KOH s. E. Clar and D. G. Stewart, Soc. *1951*, 687.

Copper chromite *$CuCr_2O_4$*

Hydrocarbons from alcohols OH → H
s. *6,* 107

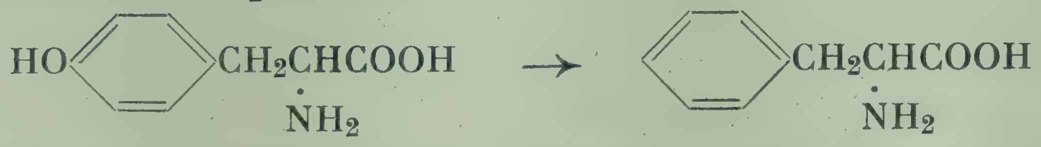
Hydriodic acid/phosphorus *HI/P*

s. *5,* 91; s. a. A. W. Ruddy and J. S. Buckley, Jr., Am. Soc. *72,* 718 (1950)

Nickel *Ni*

Hydrocarbons from phenols

140.

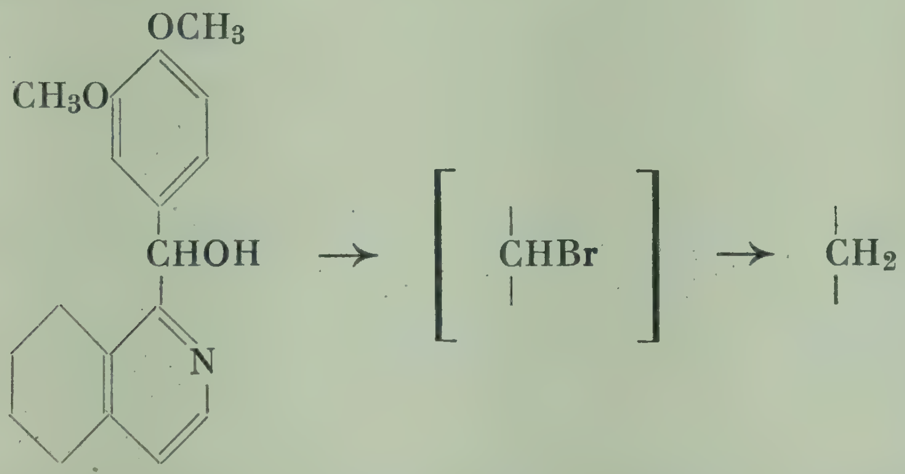


Tyrosine hydrogenated in aq. K-carbonate with Raney-Ni at 92 atm. and 196-200° → phenylalanine. Y: ca. 100%. M. Metayer, A. ch. [12] *4,* 212 (1949).

Via intermediates *v.i.*

Replacement of hydroxyl by hydrogen via bromides

141.



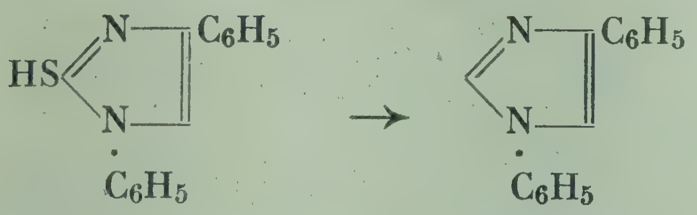
1-(α-Hydroxyveratryl)-5,6,7,8-tetrahydroisoquinoline dissolved in HBr-glacial acetic acid, allowed to stand for 24 hrs., and treated with Zn-dust at 25-30° over a period of 2 hrs. with stirring → 1-veratryl-5,6,7,8-tetrahydroisoquinoline. Y: 83%. F. e. s. R. Grewe, A. Mondon, and E. Nolte, A. *564,* 161 (1949).

Sulfur ↑ HC ⇑ S

Nitric acid/nitrous acid *HNO_3/HNO_2*

Replacement of sulfhydryl by hydrogen SH → H

142.



A soln. of $NaNO_2$ in dil. (1:3) HNO_3 added with stirring below 35° to an ice-cooled soln. of 1 gm. 1,4-diphenyl-2-thiolimidazole (prepn. s. 50) in glacial acetic acid, and stirring continued for 15 min. → 0.8 gm. crude 1,4-diphenylimidazole. R. M. Dodson and F. Ross. Am. Soc. *72*, 1478 (1950).

Carbon ↑ HC ⇑ C

Without additional reagents *w.a.r.*

Decarboxylation COOH → H

s. *6*, 135, 137

Dimethylaniline $C_6H_5N(CH_3)_3$

s. *6*, 136

Copper (II) carbonate, basic

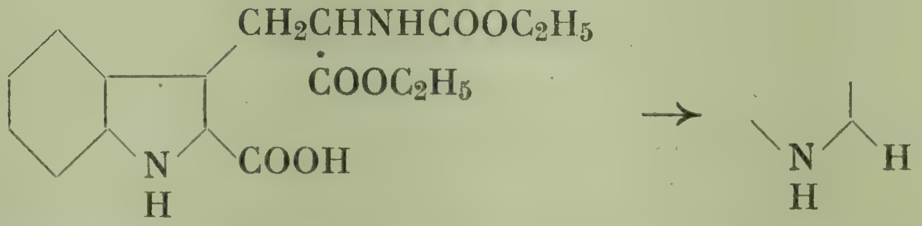
s. *1*, 113; s. a. J. W. Cook and J. S. Moffatt, Soc. *1950*, 1160

Calcium hydroxide $Ca(OH)_2$

s. *6*, 796

Resorcinol

143.

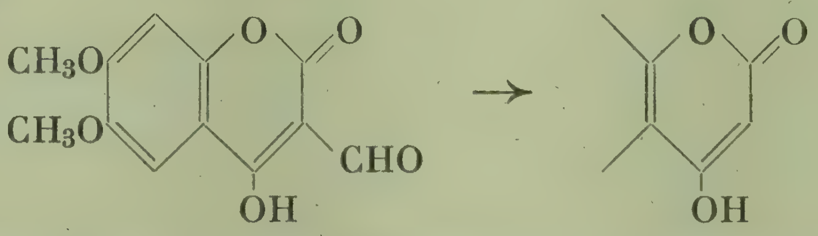


Ethyl β-(2-carboxy-3-indolyl)-α-(carbethoxyamino)propionate heated in resorcinol at 235° for 10 min. → ethyl β-(3-indolyl)-α-(carbethoxyamino)propionate. Y: 75%. H. Plieninger, B. *83*, 268 (1950).

Sulfuric acid H_2SO_4

Deformylation CHO → H

144.



1 gm. 4-hydroxy-6,7-dimethoxy-3-formylcoumarin refluxed 5 hrs. with H_2SO_4 in acetone → 0.7 gm. 4-hydroxy-6,7-dimethoxycoumarin. G. W. K. Cavill, A. Robertson, and W. B. Whalley, Soc. *1950*, 1031.

Nickel-silica $Ni\text{-}SiO_2$

Hydrocarbons from prim. alcohols $CH_2OH \rightarrow H$

Degradation with loss of 1 C-atom

145. $CH_3CH_2CH_2CH_2OH \rightarrow CH_3CH_2CH_3$

n-Butyl alcohol hydrogenated in the presence of Ni-kieselguhr catalyst at 239° and atmospheric pressure → propane. Y: 98-99%. F. e. s. V. N. Ipatieff et al., Ind. Eng. Chem. *41*, 1802 (1949).

Formation of O—N Bond

Uptake

Addition to Nitrogen ON⇓N

Perphthalic acid ←

N-Oxides N:O

as intermediates s. *6*, 389

Hydrogen peroxide H_2O_2

s. *3*, 95a; from aliphatic tert. amines s. A. C. Cope and P. H. Towle, Am. Soc. *71*, 3423 (1949)

Formation of O—S Bond

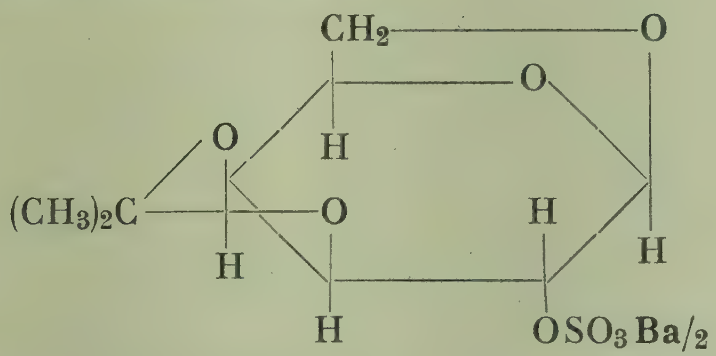
Uptake

Addition to Hydrogen and Oxygen OS⇓HO

Pyridine C_5H_5N

Carbohydrate sulfuric acid esters OH → OSO_3H

146.



Pyridine-SO_3 added with shaking to a soln. of 3,4-isopropylidene-1,6-anhydro-β-D-galactose in dry pyridine, stirred with a vigorous current of N_2 and heated at 50° for 2.5 hrs., then poured with stirring into excess of a suspension of Ba-carbonate in water → Ba-3,4-isopropylidene-1,6 anhydro-β-D-galactose-2-sulfate. Y: 89%.—This process avoids the use of large volumes of Ag_2SO_4, necessary, when $ClSO_3H$ is used, cf. Synth. Meth. *2*, 133. F. e. s. R. B. Duff, Soc. *1949*, 1597.

Steroid sulfuric acid esters

s. *1*, 122

Addition to Sulfur OS ⇓ S

Hydrogen peroxide *H_2O_2*

Sulfoxides and sulfones from thioethers $R_2S \begin{matrix}\nearrow R_2SO \\ \searrow R_2SO_2\end{matrix}$

s. *5*, 101; s. a. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, Am. Soc. *72*, 2856 (1950); P. Block, Jr., and J. L. Balmat, Am. Soc. *72*, 5638 (1950)

Sulfones from thioethers $R_2S \rightarrow R_2SO_2$

s. *1*, 117; *2*, 542, 558; *3*, 502; *5*, 101; *6*, 148; s. a. A. C. Cope, D. E. Morrison, and L. Field, Am. Soc. *72*, 59 (1950)

Iodosobenzene *C_6H_5IO*

Sulfoxides from thioethers $R_2S \rightarrow R_2SO$

147. $(HOCH_2CH_2)_2S + OJC_6H_5 \rightarrow (HOCH_2CH_2)_2SO + JC_6H_5$

12 gm. thiodiglycol in water heated on a steam bath, iodosobenzene added, and worked up after 15 min. → 11 gm. 2,2′-dihydroxydiethyl sulfoxide.—Iodosobenzene is a useful reagent for this reaction. F. e. s. A. H. Ford-Moore, Soc. *1949*, 2126.

Potassium permanganate *$KMnO_4$*

Sulfones from thioethers $R_2S \rightarrow R_2SO_2$

148. H_2O_2-oxidation of diphenyl sulfides with no substituents in o-position takes place smoothly at 50° in excellent yield. With one substituent, the oxidation gives lower yields, and with substituents in 0,0′-positions, the H_2O_2-oxidation fails completely as preparative method. The oxidation of 0,0′-disubst. compounds can, however, sucessfully be carried out by the use of $KMnO_4$ in dil. acetic acid. E. s. B. R. Baker, M. V. Querry, and A. F. Kadish, J. Org. Chem. *15*, 402 (1950).

Exchange

Hydrogen ↑ OS ⇅ H

Thionyl chloride *$SOCl_2$*

Sulfurous acid esters $(RO)_2SO$

s. *4*, 144; cf. W. Gerrard, A. Nechvatal, and B. M. Wilson, Soc. *1950*, 2088

Halogen ↑ OS ⇅ Hal

Without additional reagents *w.a.r.*

Chlorosulfinic acid esters ROSOCl

s. *4*, 144; s. a. E. M. Fry, J. Org. Chem. *14*, 887 (1949)

Sodium hydroxide *NaOH*

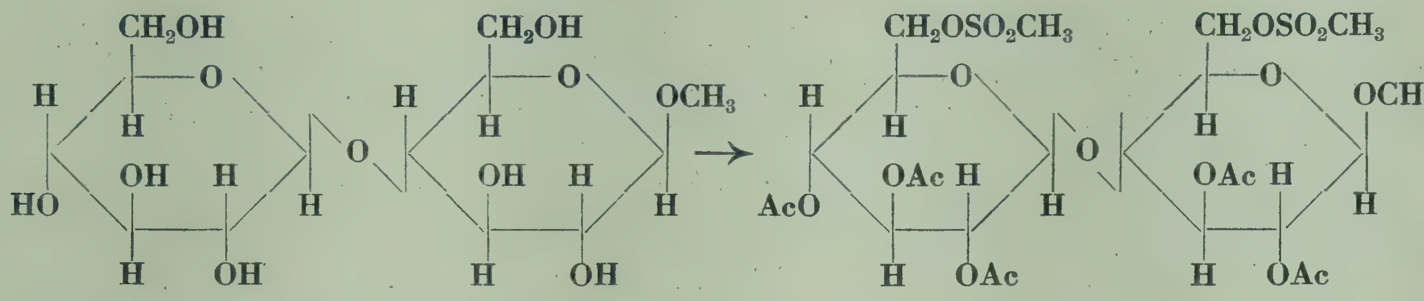
Sulfonic acid esters from sulfonic acid chlorides $SO_2Cl \rightarrow SO_2OR$

s. *4*, 212; aryl esters s. H. R. Slagh and E. C. Britton, Am. Soc. *72*, 2808 (1950)

Pyridine C_5H_5N

Methylsulfonic acid esters from alcohols ←
Selective acylation

149.


CH₂OH
O
H
H
OH
H
HO
H
H
OH
O
CH₂OH
O
OCH₃
H
H
OH
H
H
H
OH
CH₂OSO₂CH₃
O
H
H
OAc H
AcO
H
H
OAc
O
CH₂OSO₂CH₃
O
OCH₃
H
OAc H
H
H
OAc

A soln. of 11.7 gm. methyl β-cellobioside in pyridine treated at 0° with 2 moles of methanesulfonyl chloride for 12 hrs., followed by acetic anhydride for 4 hrs. at room temp. → 19 gm. methyl 6,6′-bis (methanesulfonyl)pentaacetyl β-cellobioside. F. H. Newth et al., Soc. *1949*, 2550.

Sulfonyloximes $C:NOSO_2R$

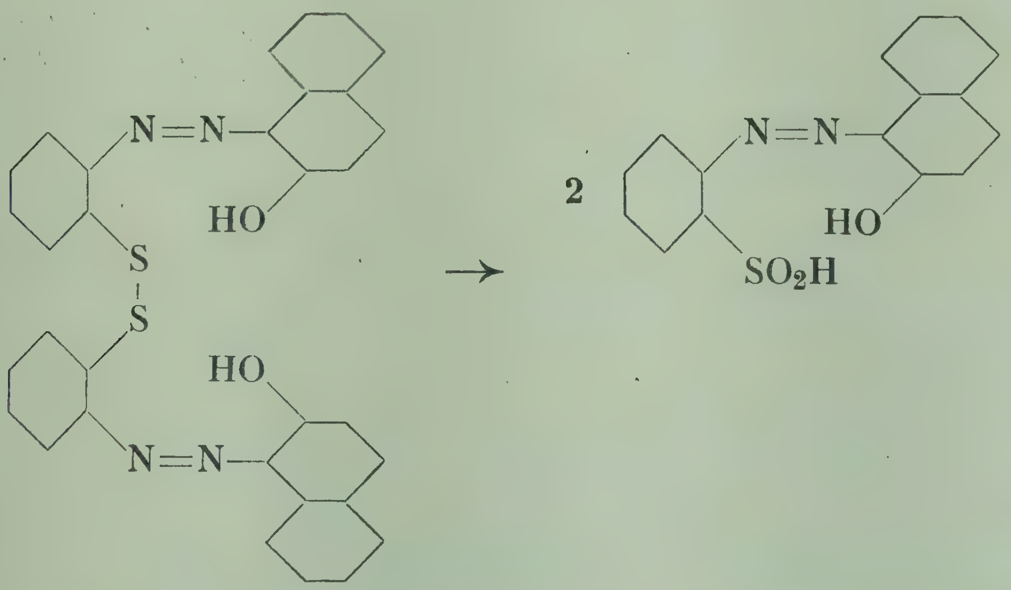
s. *4*, 143; s. a. Am. Soc. *72*, 2738 (1950)

Sulfur ↑ OS ⇅ S

Sodium hydroxide *NaOH*

Sulfinic acids from disulfides $RSSR \rightarrow 2\ RSO_2H$

150.


N=N
HO
S
S
HO
N=N
2
N=N
HO
SO₂H

Bis-o-(2-hydroxy-1-naphthylazo)phenyl disulfide refluxed 3 hrs. with NaOH in aq. ethanol (1 : 1) → o-(2-hydroxy-1-naphthylazo)benzenesulfinic acid. Y: 80%. A. Burawoy and C. Turner, Soc. *1950*, 469.

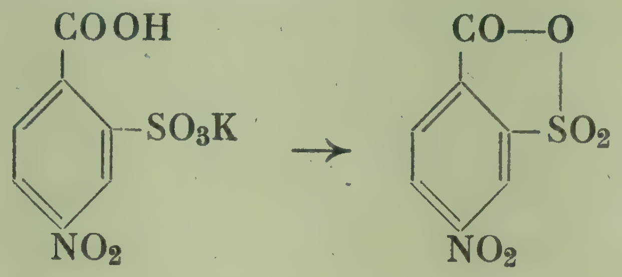
Elimination

Oxygen ↑ **OS ⇑ O**

Thionyl chloride *$SOCl_2$*

Carboxylic sulfonic acid anhydrides ←

151.



Mono-K-salt of 4-nitro-2-sulfobenzoic acid and $SOCl_2$ refluxed for 18 hrs. on a water bath → 4-nitro-2-sulfobenzoic acid endoanhydride. Y: 72%. F. methods s. C. A. Grob and M. W. Goldberg, Helv. *32*, 172 (1949).

Formation of O—Rem Bond

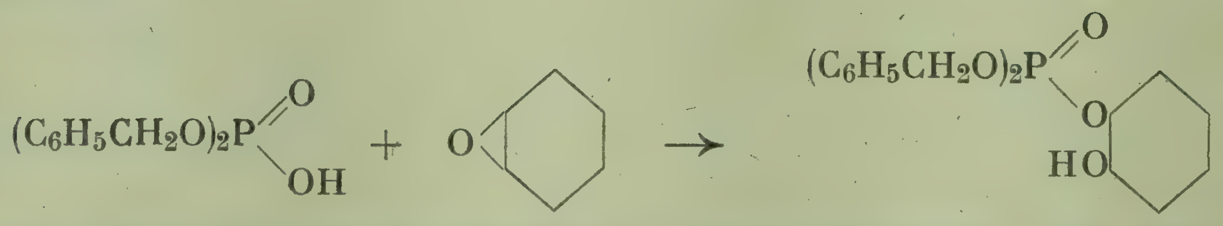
Uptake

Addition to Oxygen and Carbon **ORem ⇓ OC**

Without additional reagents *w.a.r*

Phosphoric acid esters from oxido compounds ←

152.



Di-p-nitrobenzyl hydrogen phosphate and cyclohexene oxide dissolved in dioxane, and heated on a water bath for 2 hrs. → 2-hydroxycyclohexyl di-p-nitrobenzyl phosphate. Y: 95%. F. e. s. J. Baddiley et al., Soc. *1949*, 815.

Addition to Remaining Elements **ORem ⇓ Rem**

Hydrogen peroxide *H_2O_2*

Arsine oxides from arsines ←

153. $(C_6H_5)_3As \rightarrow (C_6H_5)_3AsO$

30%-H_2O_2 added dropwise with stirring over a period of 20-30 min. at 25-30° to a soln. of triphenylarsine (prepn. s. 673) in acetone, and stirring continued for 30 min. → triphenylarsine oxide (startg. m. f. 670). Y: 84-87%. R. L. Shriner and C. N. Wolf, Org. Synth. *30*, 95 (1950).

Exchange

Hydrogen ↑ — ORem ⇅ H

Without additional reagents — *w.a.r.*

Dithiophosphoric acids — $(RO)_2 \rightarrow PSSH$

s. *6*, 156

Nitrogen ↑ — ORem ⇅ N

Without additional reagents — *w.a.r.*

Silicates from aminosilanes ←

54.

$$[(CH_3)_3C\cdot O]_2Si(NH_2)_2 + 2\ HOCH(CH_3)CH_2NH_2 \rightarrow [(CH_3)_3C\cdot O]_2Si[OCH(CH_3)CH_2NH_2]_2$$

Di-t-butoxydiaminosilane and 1-amino-2-propanol refluxed 1 hr. → di-t-butyldi-(2-amino-1-methylethyl) silicate. Y: 72%. F. e. s. P. A. Di Giorgio, L. H. Sommer, and F. C. Whitmore, Am. Soc. *71*, 3254 (1949).

Halogen ↑ — ORem ⇅ Hal

Without additional reagents — *w.a.r.*

Siloxanes from halogenosilanes ←

s. *6*, 543

Potassium hydroxide — *KOH*

Silanols from halogenosilanes — $SiCl \rightarrow SiOH$

55.

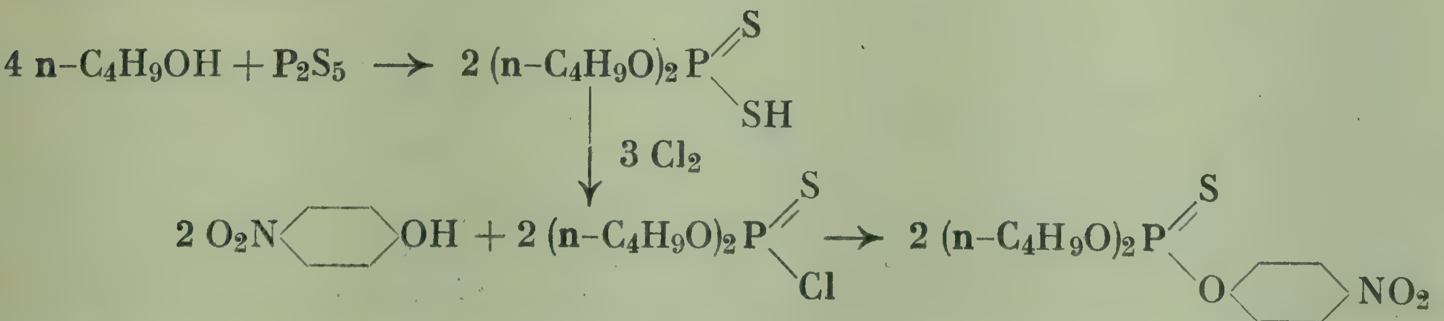
$$(C_6H_{11})_3SiCl \rightarrow (C_6H_{11})_3SiOH$$

Chlorotri(cyclohexyl)silane dissolved in boiling 5%-alc.-KOH, and worked up after a few min. → tri(cyclohexyl)silanol. Y: 87%. W. H. Nebergall and O. H. Johnson, Am. Soc. *71*, 4022 (1949).

Sodium carbonate — *Na_2CO_3*

Monothiophosphoric acid esters via dithiophosphoric acids and chlorothiophosphoric acid esters ←

56.



n-Butanol added over a period of 1.5-2.5 hrs. to a refluxing suspension of P_2S_5 in benzene, refluxing continued for 2 hrs., Cl_2 introduced at

25-30° over a period of ca. 1.5 hrs., stirred 15-20 min. more, and added to water with vigorous stirring during 30-45 min. at 25-35° 0,0-dibutyl chlorothiophosphate (Y: 64% based on P_2S_5), p-nitrophenol, and anhydrous Na-carbonate in methyl ethyl ketone refluxed 3-5 hrs. with stirring → 0,0-dibutyl-0-(p-nitrophenyl)thiophosphate (Y: 89%). F. e., using also acetone in the second step, s. J. H. Fletcher et al., Am. Soc. *72*, 2461 (1950).

Sodium salt *Na^+*

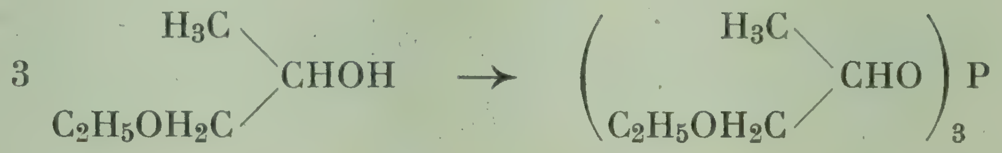
Monothiophosphoric acid esters ←

s. *4*, 147; addition of tert. amines and phosphines as catalysts s. A. D. F. Toy and T. M. Beck, Am. Soc. *72*, 3191 (1950)

Dialkylaniline *$C_6H_5NR_2$*

Phosphites ←

157.



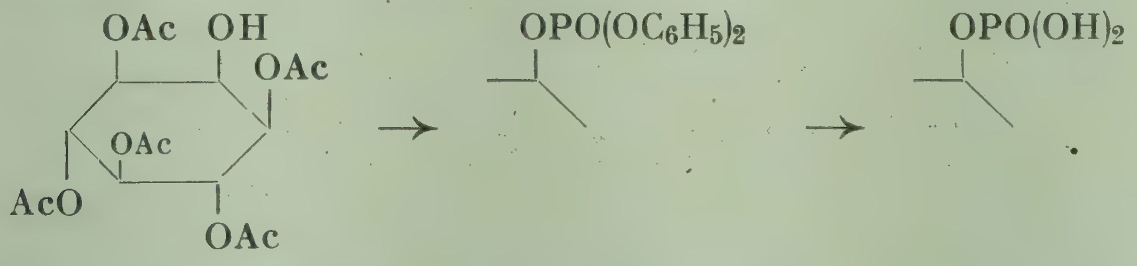
$$3\ \begin{matrix}H_3C\\C_2H_5OH_2C\end{matrix}\!\!>CHOH \rightarrow \left(\begin{matrix}H_3C\\C_2H_5OH_2C\end{matrix}\!\!>CHO\right)_3P$$

PCl_3 added dropwise with ice-cooling and stirring to a mixture of 1-ethoxy-2-hydroxypropane, dimethylaniline, and dry ether, stirring continued for 0.5 hr. → 1-ethoxy-2-propyl phosphite. Y: 70%. F. e. s. V. S. Abramov and E. N. Nikolaeva, Ж. *20*, 100 (1950); C. A. *44*, 5799 h; cf. W. Gerrard, A. Nechvàtal, and B. M. Wilson, Soc. *1950*, 2088; with diethylaniline s. A. H. Ford-Moore and B. J. Perry, Org. Synth. *31*, 111 (1951).

Pyridine *C_5H_5N*

Phosphorylation of hydroxy compounds ←
Hydrogenolysis of phosphoric acid esters

158.



3 moles of diphenylchlorophosphonate added to a soln. of 1,2,3,4,6-pentaacetylinositol in anhydrous pyridine, and the mixture kept at 80° for 20 hrs. → 1,2,3,4,6-pentaacetylinositol-5-diphenylphosphate (Y: 64%) hydrogenated in anhydrous ethanol with PtO_2 at room temp. and atmospheric pressure for 90 min. until the absorption of H_2 ceases → 1,2,3,4,6-pentaacetylinositol-5-phosphoric acid (startg. m. f. 14) (Y: 80%). B. M. Iselin, Am. Soc. *71*, 3822 (1949); s. a. K. R. Farrar, Soc. *1949*, 3131; K. M. Mann and H. A. Lardy, J. Biol. Chem. *187*, 339 (1950).

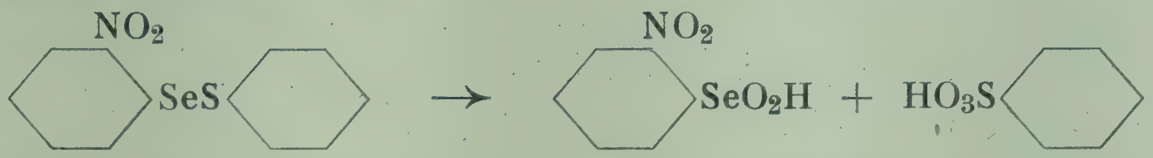
Phosphorylcholines ←
s. *5,* 108; s. a. Am. Soc. *72,* 942 (1950)

Sulfur ↑ **ORem ⇅ S**

Hydrogen peroxide H_2O_2

Seleninic acids and sulfonic acids from selenylsulfides ←

59.



Excess 30%-H_2O_2 added to a soln. of o-nitrophenylselenyl phenyl sulfide (prepn. s. 602) in glacial acetic acid allowed to stand 2 hrs. at room temp. and evaporated on a water bath until the odor of acetic acid disappears → o-nitrobenzeneseleninic acid (Y: 91.9%) and benzenesulfonic acid (Y: 91.7%). H. Reinboldt and E. Giesbrecht, A. *568,* 198 (1950).

Formation of O—C Bond

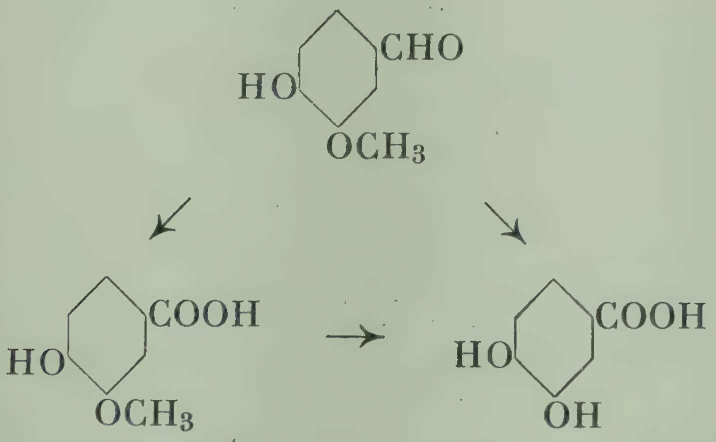
Uptake

Addition to Hydrogen and Carbon **OC ⇓ HC**

Sodium hydroxide/potassium hydroxide *NaOH/KOH*

Carboxylic acids from aldehydes, also cleavage of ethers CHO → COOH

60.



Vanillin added slowly with stirring at 165–200° to a mixture of NaOH and KOH in some water

and stirred an additional 5 min. → vanillic acid. Y: 98%.	and heated at 250° for 1 hr. → protocatechuic acid. Y: 99%.

F. more details s. I. A. Pearl and D. L. Beyer. Ind. Eng. Chem. *42,* 376 (1950); s. a. Org. Synth. *29,* 85 (1949); *30,* 103 (1950)

Sodium nitrite/nitric acid s. Nitric acid/sodium nitrite $NaNO_2/HNO_3$

Copper acetate/nickel acetate s. Nickel acetate/copper acetate ←

Silver nitrate/sodium hydroxide *$AgNO_3/NaOH$*

Carboxylic acids from aldehydes CHO → COOH

s. *3,* 112; s. a. J. C. Sheehan and C. A. Robinson, Am. Soc. *73,* 1207 (1951)

Nitric acid/sodium nitrite *$HNO_3/NaNO_2$*

Carboxylic acids from aldehydes

s. *6,* 170

Persulfate *$S_2O_8^{--}$*

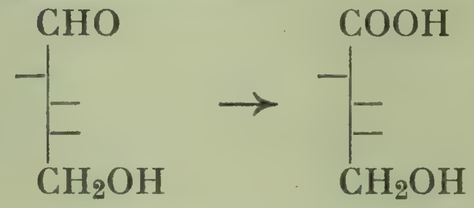
Replacement of hydrogen by hydroxyl H → OH
Elbs oxidation

s. *1,* 131; s. a. J. Forrest and V. Petrow, Soc. *1950,* 2340

Bromine *Br*

Aldonic acids from carbohydrates CHO → COOH

161.



Br_2 added to an aq. soln. of D-arabinose, kept for 2 hrs., excess Br_2 removed by aeration, the HBr formed removed by Ag_2O, any Ag^+ in soln. precipitated with H_2S and the soln. boiled 15 min. with Ca-carbonate → Ca-D-arabonate. Y: 85.2%. L. F. Wiggins et al., Soc. *1949,* 1358; also in the presence of $CaCO_3$ s. Soc. *1949,* 1879

Nickel acetate/copper acetate ←

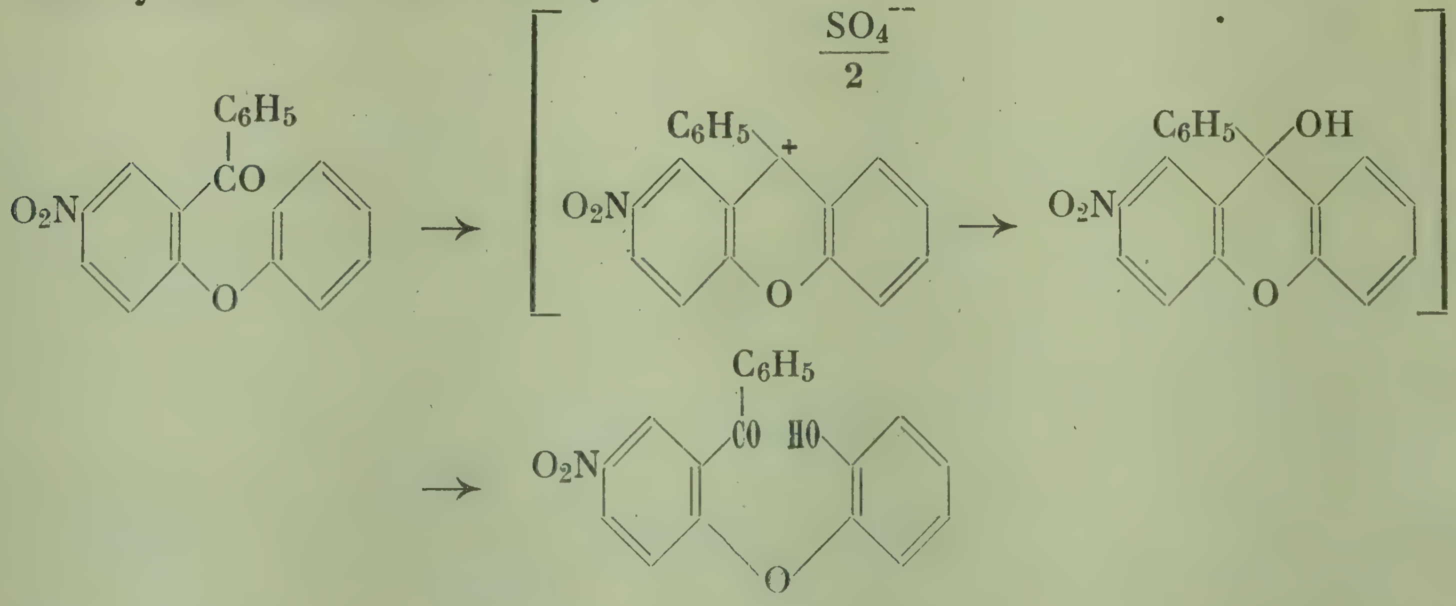
Carboxylic acids from aldehydes ←

s. *6,* 292

Via intermediates *v.i.*

o-Hydroxyethers from ethers via xanthylium salts and xanthydrols ←

162.



5-Nitro-2-phenoxybenzophenone dissolved in cold concd. H_2SO_4, after 30 min. acetic acid added, then H_2O_2 added during 5 min. with vigorous stirring but without external cooling, and kept at room temp. for 3 hrs. → 5-nitro-2-o-hydroxyphenoxybenzophenone. Y: almost 100%. F. e., also with isolation of the intermediates, s. J. D. Loudon et al., Soc. *1950*, 55.

Addition to Oxygen and Carbon OC ⇓ OC

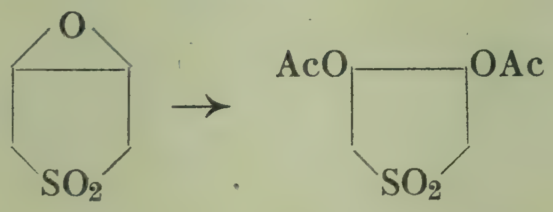
Without additional reagents *w.a.r.*

Partial and mixed dicarboxylic acid derivatives C

s. *3*, 114; s. a. F. E. King, B. S. Jackson, and D. A. A. Kidd, Soc. *1951*, 243

Glycol esters from oxido compounds

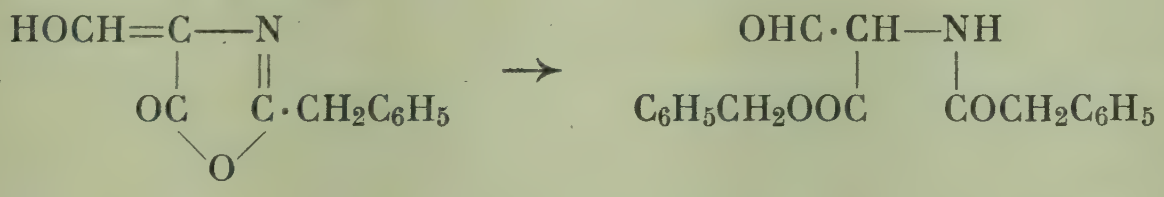
63.



Butadiene sulfone epoxide and acetic acid heated 12 hrs. at 210° → 3,4-diacetoxythiacyclopentane 1,1-dioxide. Y: 83%. O. E. van Lohuizen and H. J. Backer, R. *68*, 1137 (1949).

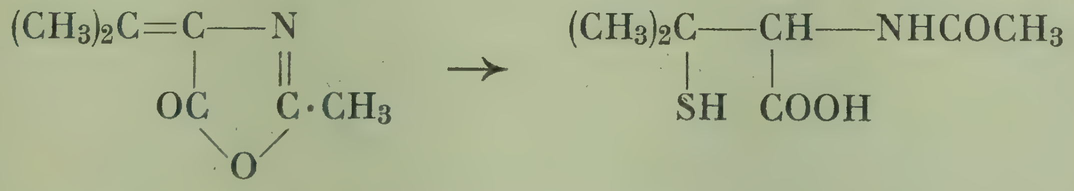
Oxazolone ring opening

64.



A mixture of 2-benzyl-4-hydroxymethylene-5-oxazolone, benzyl alcohol, and dry benzene refluxed for ca. 45 min. → benzyl benzylpenaldate. Y: 90%. F. e. s. E. V. Brown, Chemistry of Penicillin *1949*, 508; s. a. Synth. Meth. *4*, 804.

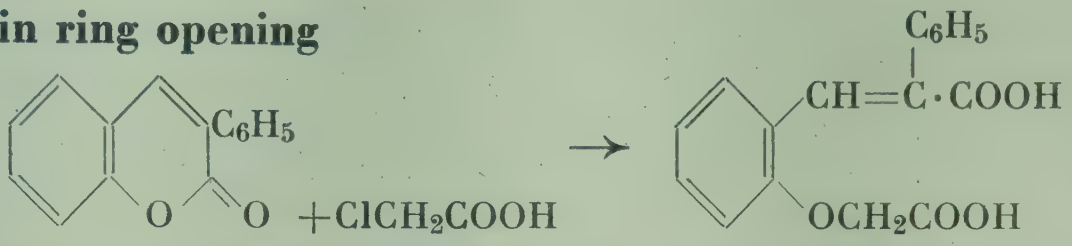
65.



Methanol satd. at 0° with H_2S in a pressure bottle, freshly distilled 4-isopropylidene-2-methyl-5(*4H*)-oxazolone added, stoppered, allowed to stand overnight at room temp., evaporated in vacuo, and the residue heated with water at 90° for 15 min. → N-acetyl-DL-penicillamine. Y: 80%. H. M. Crooks, Jr., Chemistry of Penicillin *1949*, 455.

Coumarin ring opening

166.

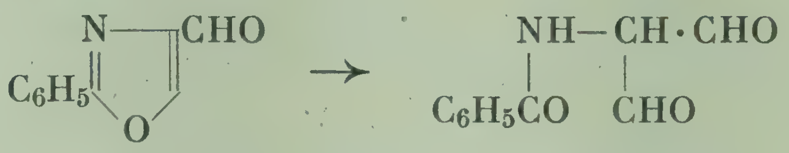


3-Phenylcoumarin treated with NaOH and excess Na-chloroacetate → α-phenylcoumarinic acid-O-acetic acid. Y: 93%. F. e. s. C. F. Koelsch and C. R. Stephens, Jr., Am. Soc. *72*, 2209 (1950).

Sodium hydroxide *NaOH*

Oxazole ring opening

167.



2 gm. 2-phenyloxazole-4-aldehyde boiled 2 min. with 2 *N* NaOH until dissolved → 2 gm. benzamidomalondialdehyde. F. e. s. J. W. Cornforth et al., Soc. *1949*, 1549; cf. Synth. Meth. *6*, 197.

Sodium alkoxide *NaOR*

Oxazolone ring opening
s. *6*, 757

Boron fluoride *BF_3*

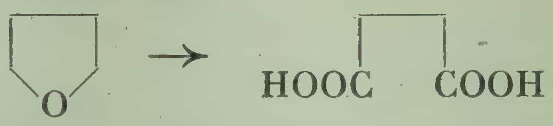
Triacoxyisocyclics from quinones ←
Thiele reaction
s. *5*, 121; s. a. D. J. Cram, Am. Soc. *71*, 3953 (1949)

Peracetic acid/cobalt(II)-acetate
s. Cobalt(II)-acetate/peracetic acid *$CH_3COO_2H/(CH_3COO)_2Co$*

Nitrous acid/nitric acid *HNO_2/HNO_3*

Oxidative furan ring opening

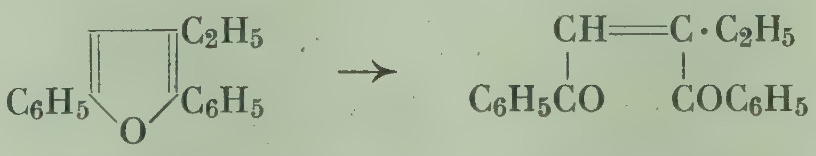
168.



Tetrahydrofuran and 10.5 *N* HNO_3, containing a little $NaNO_2$, kept at 8^0 for 15 hrs. → succinic acid. Y: 84%. F. details s. H. Schmid, A. Maschka and H. Frauenschill, M. *80*, 670 (1949).

Nitric acid *HNO_3*

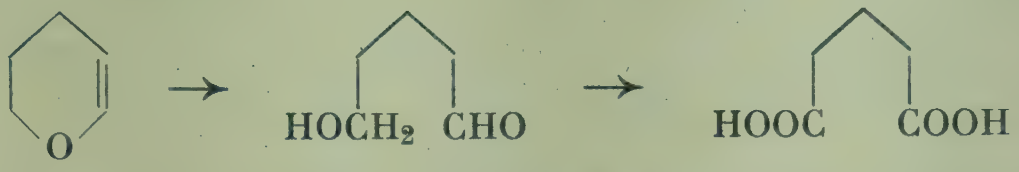
169.



A suspension of 3-ethyl-2,5-diphenylfuran in glacial acetic acid treated with a soln. of HNO_3 in glacial acetic acid, and worked up after 20 min. → 1,2-dibenzoyl-1-butene. Y: 74%. F. e. s. P. S. Bailey and W. W. Hakki, Am. Soc. *71*, 2886 (1949).
s. *5*, 122; s. a. P. S. Bailey and J. D. Christian, Am. Soc. *71*, 4122 (1949)

Glutaric acids
Pyran ring opening

170.

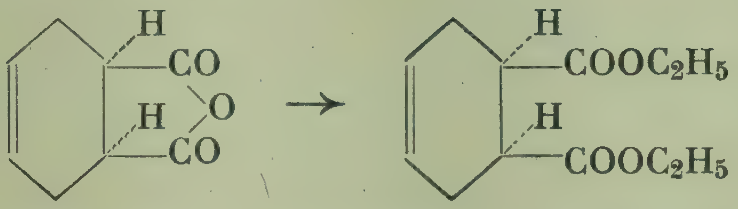


A mixture of dihydropyran and 0.2 *N* HNO_3 heated 0.5-1 hr. on a steam bath with swirling after 25-45 min. to aid dissolution, the δ-hydroxyvaleraldehyde soln. so obtained added with cooling to concd. HNO_3 containing $NaNO_2$, stirring continued for 90 min. with cooling, then the temp. allowed to rise to 25-30°, and worked up when the color has turned light yellow after 2-3 hrs. → glutaric acid. Y: 70-80%. J. English, Jr., and J. E. Dayan, Org. Synth. *30*, 48 (1950).

p-Toluenesulfonic acid *TsOH*

Dicarboxylic acid esters from dicarboxylic acid anhydrides

171.

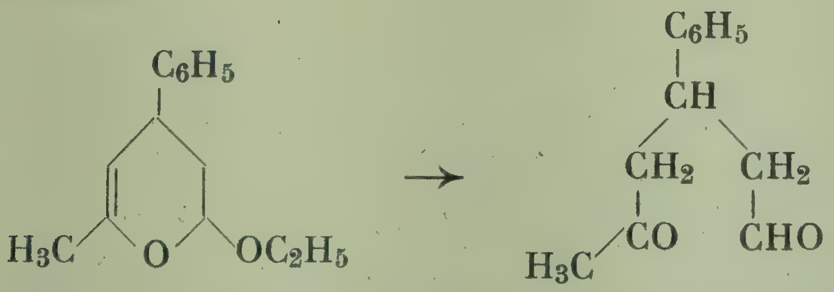


*cis-Δ*⁴-Tetrahydrophthalic anhydride, commercial abs. ethanol, and some p-toluenesulfonic acid monohydrate refluxed 12-16 hrs. at an oil bath temp. of 95-105°, toluene added, distilled; when the vapor temp. begins to drop, more ethanol added, and refluxing with subsequent azeotropic distillation repeated → diethyl *cis-Δ*⁴-tetrahydrophthalate. Y: 83-86%. F. e. s. A. C. Cope and E. C. Herrick, Org. Synth. *30*, 29 (1950); Am. Soc. *72*, 983 (1950); s. a. E. C. Schreiber and E. J. Becker, Am. Soc. *72*, 4829 (1950).

Hydrochloric acid *HCl*

Pyran ring opening

172.

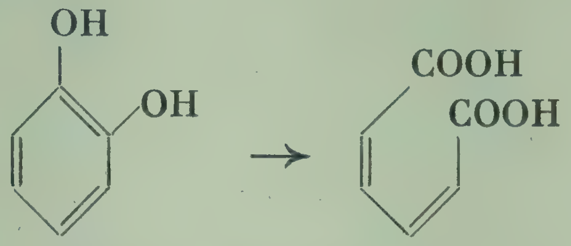


2-Ethoxy-6-methyl-4-phenyl-3,4-dihydro-2H-pyran (prepn. s. 696) and HCl in acetone-water warmed at 35° until it becomes homogeneous and thereafter at 40° for 1 hr. → 5-oxo-3-phenylhexanal. Y: 85%. F. e. s. R. I. Longley, Jr., and W. S. Emerson, Am. Soc. *72*, 3079 (1950).

Cobalt(II)-acetate/peracetic acid *$(CH_3COO)_2Co/CH_3COO_2H$*

Oxidative ring opening

173.



A soln. of peracetic acid in glacial acetic acid added at 0-10° with stirring and cooling to a soln. of pyrocatechol in glacial acetic acid, after 10 min. a soln. of Co(II)-acetate in glacial acetic acid added, and worked up after 4-5 days → muconic acid. Y: 65-85%.—With more peracetic acid muconyl acetyl peroxide is formed in a yield of 60-66%. A. Wacek and R. Fiedler, M. *80*, 170 (1949).

Addition to Nitrogen and Carbon OC ⇓ NC

Without additional reagents *w.a.r.*

Acylcarbamates from isocyanates NCO → NHCOOAc

174. $2\ CH_3COOH + OCN[CH_2]_6NCO \rightarrow CH_3CO\cdot O\cdot CONH[CH_2]_6NHCO\cdot O\cdot COCH_3$

50 gm. glacial acetic acid added dropwise at 8-15° to a soln. of 50 gm. hexamethylene di-isocyanate in benzine, and filtered by suction after ¾ hrs. → 80 gm. diacetyl hexamethylenedicarbamate. F. e. s. S. Petersen, A. *562*, 205 (1949).

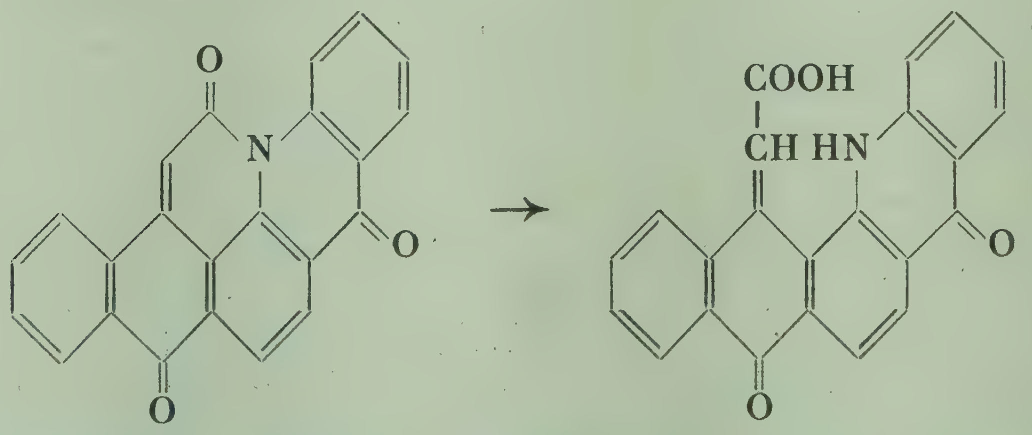
Sodium hydroxide *NaOH*

Pseudobases ←

s. *6*, 820

Pyridone ring opening C

175.

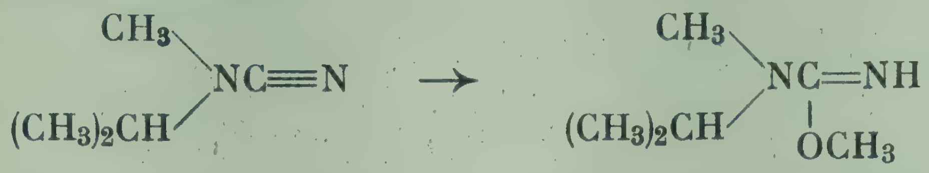


Anthrapyridonacridone boiled in 10% aq.-alc. (1 : 1) NaOH for 5 min. → 9-methyleneanthronacridone-ω-carboxylic acid. Y: 84.6%. F. e. s. A. M. Lukin and P. M. Aronovich, Ж. *19*, 362 (1949); C. A. *44*, 1080c.

Sodium/alcohol *NaOR*

Isoureas from cyanamides ←

176.



12.1 gm. methylisopropylcyanamide added to a soln. of Na in methanol, and stirred 2 hrs. at 50-55° → 10.4 gm. O,N-dimethyl-N-isopropylisourea. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, Soc. *1949*, 1732.

Triethylamine *$(C_2H_5)_3N$*

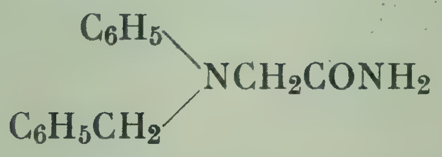
Urethans from phenols OH → OCONHR

s. *5*, 125; s. a. J. M. Lyons and R. M. Thomson, Soc. *1950*, 1971

Sulfuric acid *H_2SO_4*

Carboxylic acid amides from nitriles CN → $CONH_2$

177.



Cold N-benzyl-N-phenylglycinonitrile added dropwise to concd. H_2SO_4 cooled to — 8°, and allowed to stand 72 hrs. at room temp. → N-benzyl-N-phenyl-glycinamide. Y: 90%. F. e. s. R. A. Turner and C. Djerassi, Am. Soc. *72*, 3081 (1950).

Potassium ferricyanide *$K_3[Fe(CN)_6]$*

2-Pyridone ring from N-alkylpyridinium ring ←

s. *2*, 264; *3*, 226; s. a. V. Petrow and W. R. Wragg, Soc. *1950*, 3516

Addition to Sulfur and Carbon OC ⇓ SC

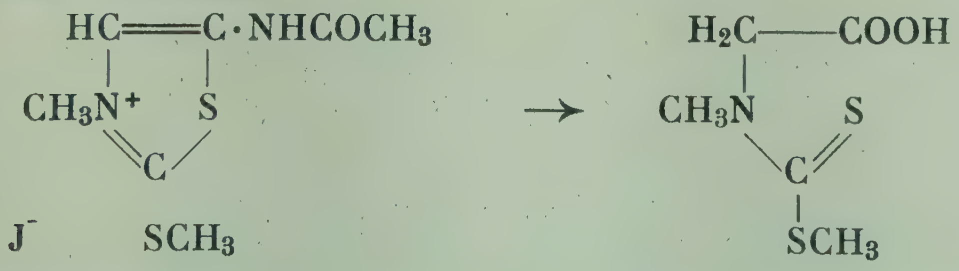
Hydrochloric acid *HCl*

Piperidone ring opening

s. *4*, 159; s. a. R. Gaudry and L. Berlinguet, Can. J. Research *28 B*, 245 (1950)

Thiazole ring opening

178.



2-Methylmercapto-3-methylthiazolium iodide (prepn. s. 378) refluxed 1 hr. with 2 *N* HCl → N-dithiocarbomethoxy-N-methylglycine. Y: 86%. F. e. s. A. H. Cook and S. F. Cox, Soc. *1949*, 2337.

Addition to Carbon OC ⇓ CC

Sodium *Na*

Ethers from ethylene derivatives C:C → CHC(OR)

179. cf. Synth. Meth. *3*, 128.
The order of activity in the addition of hydroxy compounds to alkyl acrylates is phenols ⟩ prim. alcohols ⟩ sec. alcohols. Tert. alcohols did not react. E. s. C. E. Rehberg and M. B. Dixon, Am. Soc. *72*, 2205 (1950).

s. a. D. D. Coffman et al., J. Org. Chem. *14*, 747 (1949); fluoro compounds s. A. L. Henne and M. A. Smook, Am. Soc. *72*, 4378 (1950)

Alkali hydroxide ←

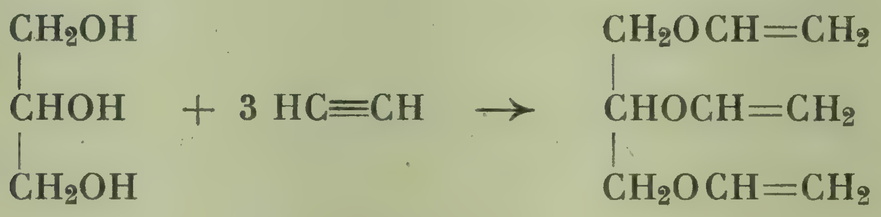
Dicarboxylic acids and cyclic ketones from β-ketocarboxylic acid esters ←

s. *2*, 160; s. a. R. Fusco and R. Trave, G. *80*, 496 (1950)

Potassium hydroxide *KOH*

Vinyl ethers ←

180.



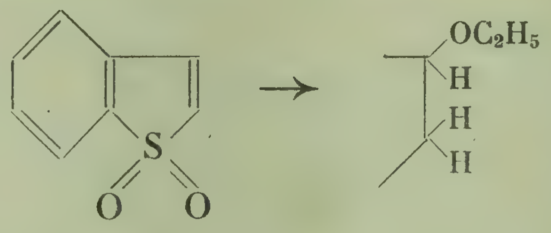
$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3\,HC{\equiv}CH \rightarrow \begin{array}{l} CH_2OCH{=}CH_2 \\ | \\ CHOCH{=}CH_2 \\ | \\ CH_2OCH{=}CH_2 \end{array}$$

Glycerol, powdered KOH, and acetylene heated at 180-190° and 10 atm. in a rotating autoclave, with repeated addition of acetylene until absorption stops → glyceryl trivinyl ether. Y: 90.3%. M. F. Shostakovskii and E. P. Gracheva, Ж. *19*, 1250 (1949); C. A. *44*, 3439a.

Potassium hydroxide in alcohol

3-Alkoxythianaphthene 1,1-dioxides, 2,3-dihydro- from thianaphthene 1,1-dioxides C:C → CHC(OR)

181.

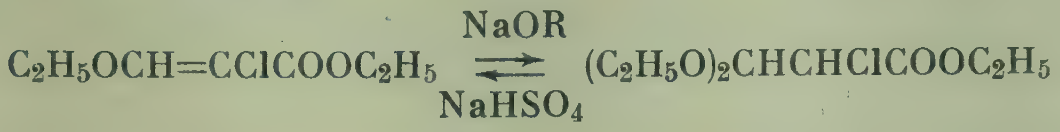


The 2-3 bond in thianaphthene 1,1-dioxide has no aromatic character and gives reactions typical of an α,β-unsatd. sulfone.—E: A soln. of thianaphthene 1,1-dioxide, KOH, and ethanol refluxed 24 hrs. → 3-ethoxy-2,3-dihydrothianaphthene 1,1-dioxide. Y: 94%. F. e. s. F. G. Bordwell and W. H. McKellin, Am. Soc. *72*, 1985 (1950).

Sodium/alcohol *NaOR*

Acetals from enolethers ←
α-Halogenacetals
Enolethers from acetals

182.



$$C_2H_5OCH{=}CClCOOC_2H_5 \underset{NaHSO_4}{\overset{NaOR}{\rightleftarrows}} (C_2H_5O)_2CHCHClCOOC_2H_5$$

A soln. of a small amount of Na in anhydrous ethanol added to an alc. soln. of ethyl α-chloro-β-ethoxyacrylate, warmed to 60°, and held at 50-60° for 1 hr. → ethyl α-chloro-β,β-diethoxypropionate (Y: 69.7 to 77%) distilled from $NaHSO_4$ → ethyl α-chloro-β-ethoxyacrylate (Y: 66.5%). W. J. Croxall and M. F. Fegley, Am. Soc. *72*, 2888 (1950).

Pyridine *C_5H_5N*

Lactolesters from hydroperoxides ←

s. *5*, 133; also isolation of the intermediate acyl peroxide s. A. C. Cope and G. Holzman, Am. Soc. 72, 3062 (1950)

Silver benzoate/iodine *C_6H_5COOAg/I*

Glycols from ethylene derivatives C:C → C(OH)C(OH)
Stereoisomers

183. **Stereoisomers.** The reaction of ethylene derivatives with Prévost reagent (Ag-benzoate, iodine) is stereospecific and yields the *trans*-isomer. M. Sletzinger and C. R. Dawson, J. Org. Chem. *14*, 849 (1949); cf. Synth. Meth. *1*, 146.

Performic acid *$HCOO_2H$*

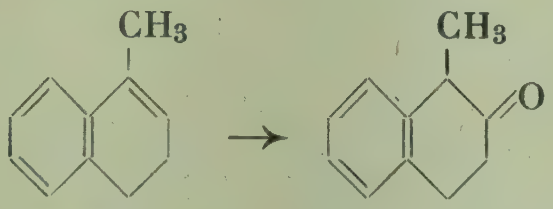
s. *5*, 138; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. *71*, 3938 (1949); J. B. Brown, H. B. Henbest, and E. R. H. Jones, Soc. *1950*, 3634

Peracetic acid/ozone s. Ozone/peracetic acid *CH_3COO_2H/O_3*

Perbenzoic acid *$C_6H_5COO_2H$*

Ketones from ethylene derivatives C:CH → CHCO

184.



A soln. of 4-methyl-1,2-dihydronaphthalene in chloroform added with ice-cooling to a soln. of perbenzoic acid in chloroform, and worked up after 3 hrs. → 4-methyl-3-tetralone. Y: 84%. H. Hock, Shon Lang, and G. Knauel, B. *83*, 227 (1950); s. a. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. *15*, 1197 (1950).

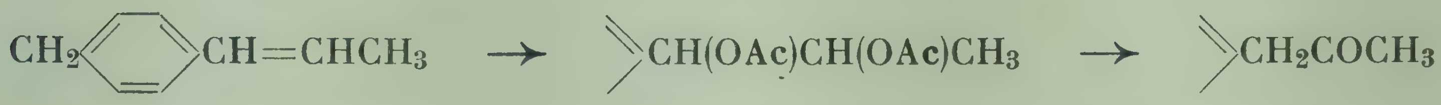
Carboxylic acid esters from ketones ←

s. *4*, 169; modification and simultaneous protection of a carbon carbon double bond s. P. Wieland and K. Miescher, Helv. *32*, 1768, 1922 (1949); stereoisomers s. R. B. Turner, Am. Soc. *72*, 878 (1950)

Red lead oxide *Pb_3O_4*

via glycol diacetates

185.



Anethole reacted with Pb_3O_4 in glacial acetic acid below 40°, and the glycol acetate so obtained boiled 4 hrs. with 20%-H_2SO_4 → anisylacetone. Y: 65%. A. Buzas and C. Dufour, Bl. *1950*, 139.

Lead tetraacetate/potassium carbonate *$(CH_3COO)_4Pb/K_2CO_3$*

Oxidative ring opening ↻

s. *6*, 842

Ammonium vanadate ←

s. *4*, 170; s. a. J. Golé, Bl. *1949*, 894.

Ozone *O_3*

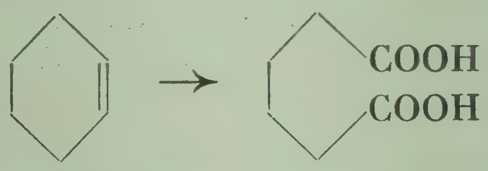
of indoles

s. *2*, 168; s. a. C. Mentzer, D. Molho, and Y. Berguer, Bl. *1950*, 782

Ozone/peracetic acid *O_3/CH_3COO_2H*

Oxidative ring opening
Cleavage of ozonides

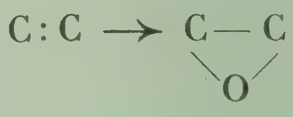
186.



Cyclohexene ozonized at —50° in methyl acetate, then peracetic acid in glacial acetic acid added, the low boiling solvent distilled off at 50° under slightly reduced pressure, more peracetic acid added, kept 12 hrs. at 50-60°, finally refluxed 1 hr. → adipic acid. Y: 86.2-90.3%. F. e. s. H. Wilms, A. *567*, 96 (1950).

Hydrogen peroxide *H_2O_2*

α,β-Oxidoketones from chalcones



s. *6*, 192, 901

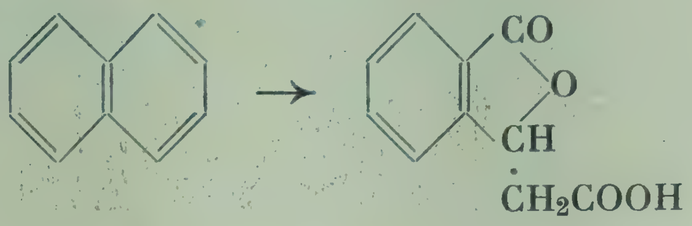
o-Hydroxyethers from xanthydrols ←

s. *6*, 162

Hydrogen peroxide/ammonium molybdate H_2O_2/NH_4MoO_4

Phthalides from naphthalene ring C
Oxidative ring opening

187.

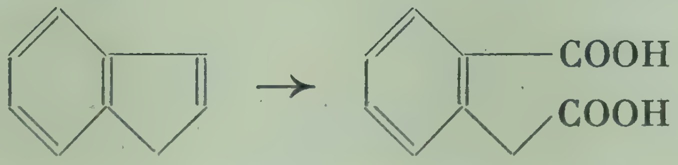


30%-H_2O_2 slowly added over a period of 4 hrs. to a gently refluxing soln. of naphthalene and NH_4-molybdate in glacial acetic acid → β-hydroxy-β-o-carboxyphenylpropionic acid lactone. Y: 69% (43% without molybdate). I. D. Raake-Fels et al., J. Org. Chem. *15*, 627 (1950).

Chromic acid CrO_3

Oxidative ring opening

188.



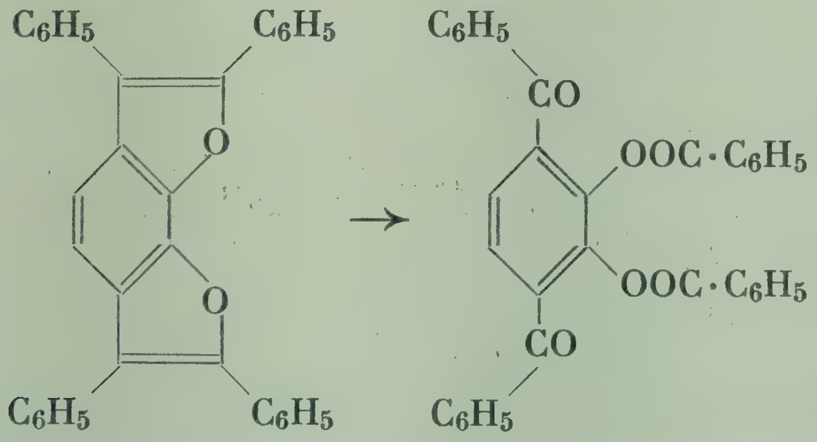
Technical ca. 90%-indene added dropwise at 65 ± 2° to an aq. soln. of $K_2Cr_2O_7$ and H_2SO_4, then stirred 2 hrs. more at the same temp. → homophthalic acid (startg. m. f. 297). Y: 66-77%. O. Grummitt, R. Egan, and A. Buck, Org. Synth. *29*, 49 (1949); acenaphthene ring opening s. H. E. Nürsten and A. T. Peters, Soc. *1950*, 729.

Ketocarboxylic acids

s. *4*, 173; s. a. J. R. Schaeffer and A. O. Snoddy, Org. Synth. *31*, 3 (1951)

Furan ring opening

189.



10% excess CrO_3 added to a boiling suspension of tetraphenyl-o-benzodifuran in glacial acetic acid over a period of 1 hr., and boiling continued for 15 min. → 2,3-bis(benzoxy)-1,4-dibenzoylbenzene. Y: almost 100%. Also partial ring opening s. O. Dischendorfer et al., Ж. *80*, 741 (1949); *81*, 725 (1950); *82*, 1 (1951).

Pertungstic acid *WoO_3*

Glycols from ethylene derivatives C:C → C(OH)C(OH)
cis-trans-Isomers

190. Whereas OsO_4 gives *cis*-glycols, WoO_3, V_2O_5, and SeO_2 give *trans*-glycols.—E: A mixture of cyclohexene, 30%-H_2O_2, WoO_3, and glacial acetic acid stirred 5-6.5 hrs. at 50° → *trans*-1,2-cyclohexanediol. Y: 74% (77% in the presence of 2 drops H_2SO_4). F. e. s. M. Mugdan and D. P. Young, Soc. *1949*, 2988.

Iodine/silver benzoate s. Silver benzoate/iodine *I/C_6H_5COOAg*

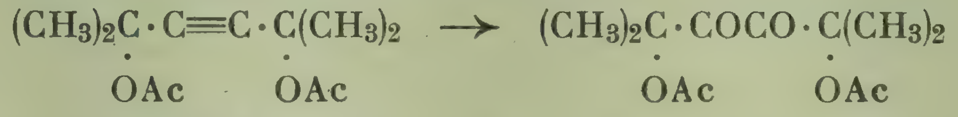
Hydrochloric acid *HCl*

β-Alkoxyacetals from α,β-ethylene aldehydes ←
s. *6*, 220

Potassium permanganate *$KMnO_4$*

α-Diketones from acetylene derivatives C⁝C → COCO

191.



$$(CH_3)_2\underset{OAc}{C}\cdot C\equiv C\cdot \underset{OAc}{C}(CH_3)_2 \rightarrow (CH_3)_2\underset{OAc}{C}\cdot COCO\cdot \underset{OAc}{C}(CH_3)_2$$

2,5-Dimethyl-3-hexyne-2,5-diol diacetate and $KMnO_4$ in water stirred ca. 2 hrs. with ice-water cooling → 2,5-dimethylhexane-3,4-dione-2,5-diol diacetate. Y: 67%. G. Dupont, R. Dulou, and D. Lefort, Bl. *1949*, 789.

Osmium tetroxide *OsO_4*

Pyrazine ring degradation ⊂
s. *6*, 41

Rearrangement

Hydrogen/Oxgen Type OC⌒HO

Hydrogen halides *HHal*

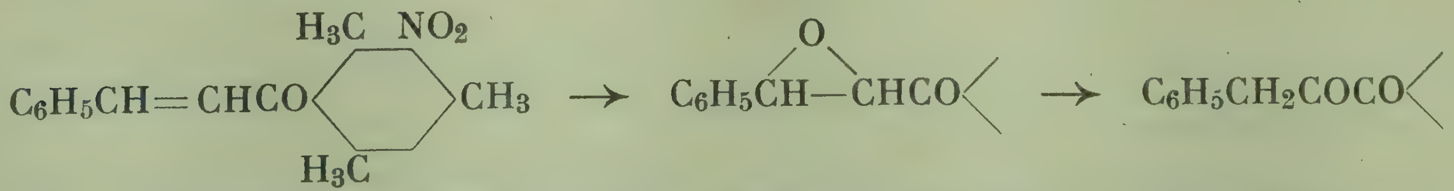
Lactones from ethylenecarboxylic acids ←
s. *5*, 149; s. a. Am. Soc. *72*, 514 (1950)

Hydrogen/Carbon Type OC⌒HC

Potassium hydroxide *KOH*

α-Diketones from chalcones via COCO
α,β-oxidoketones

192.



15%-H_2O_2 added at 20° to a soln. of benzal-3-nitroacetomesitylene in alcohol containing an equivalent amount of 6 *N* KOH, and stirring continued for 1.5 hrs. → 1-(3-nitromesitoyl)-2-phenylethylene oxide (Y: 86%) dissolved in alcohol, and boiled 1.5 hrs. with 1.5 mole *N* KOH → 3-nitromesitoyl benzyl ketone (Y: 75%). F. e. s. R. P. Barnes and L. A. Gist, Jr., Am. Soc. *72*, 2509 (1950).

Zinc *Zn*

Ketones from glycol acetates ←
Serini reaction

from monoacetates s. *5*, 150; from diacetates s. C. Djerassi and C. R. Scholz, Am. Soc. *71*, 3962 (1949)

Titanium tetrachloride $TiCl_4$

Change of configuration of carbohydrates ←

93. Cyclohexyl tetraacetyl-β-glucoside and $TiCl_4$ in abs. chloroform gently refluxed for not more than 75 min. → cyclohexyl tetraacetyl-α-glucoside. Y: 80%. E. Pascu, Am. Soc. *52*, 2568 (1930); s. a. B. Lindberg, Acta Chem. Scand. *3*, 151 (1949).

Ammonium polysulfide $(NH_4)_2S_x$

Carboxylic acid amides and carboxylic acids from methyl ketones
Willgerodt reaction

$$\mathrm{COCH_3} \begin{array}{l} \nearrow \mathrm{CH_2CONH_2} \\ \searrow \mathrm{CH_2COOH} \end{array}$$

s. *1*, 151/2; *2*, 180/a; s. a. E. V. Brown and J. A. Blanchette, Am. Soc. *72*, 3414 (1950)

Sulfuric acid H_2SO_4

Ketones from glycol acetates

$$\mathrm{CH(OAc)CH(OAc)} \rightarrow \mathrm{CH_2CO}$$

s. *6*, 185

Via intermediates *v.i.*

Carboxylic acids from methylketones via thioamides
Willgerodt-Kindler reaction

$$\mathrm{COCH_3} \rightarrow \mathrm{COOH}$$

s. *2*, 181; *3*, 141; s. a. C. C. Price and B. D. Halpern, Am. Soc. *73*, 818 (1951)

Interconversion via oxazolines ←

s. *5*, 154; s. a. Am. Soc. *73*, 1216 (1951); trans-cis rearrangement s. S. Winstein and R. Boschan, Am. Soc. *72*, 4669 (1950)

Oxygen/Carbon Type

OC↶OC

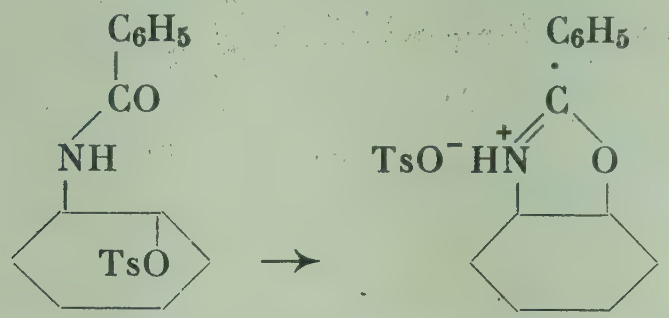
Acetic acid

CH_3COOH

Oxazoline ring

○

194.



trans-2-Benzamidocyclohexyl p-toluenesulfonate heated several min. in glacial acetic acid → 2-phenyl-4,5-tetramethyleneoxazolinium p-toluenesulfonate. Y: 95%. S. Winstein, L. Goodman, and R. Boschan, Am. Soc. *72*, 2311 (1950).

Nitrogen/Carbon Type

OC↶NC

Without additional reagents

w.a.r.

Aminocarboxylic acid esters from betaines

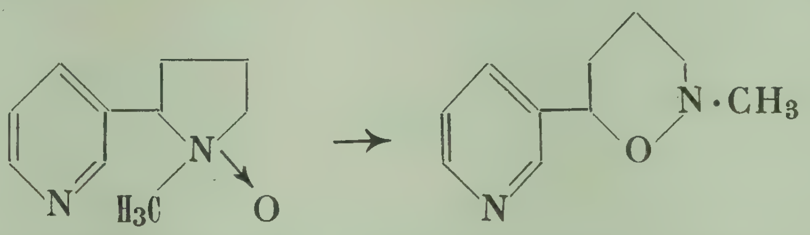
←

s. *6*, 222

1,2-Oxazines from pyrrole N-oxides
Ring enlargement

←

195.



Nicotine oxide distilled at an oil bath temp. of 190-200° and 1 mm. pressure, and the reaction product isolated as dihydrochloride → 2-methyl-6-(3-pyridyl)tetrahydro-1,2-oxazine (startg. m. f. 28). Y: 57 %. C. H. Rayburn, W. Harlan, and H. R. Hanmer, Am. Soc. *72*, 1721 (1950).

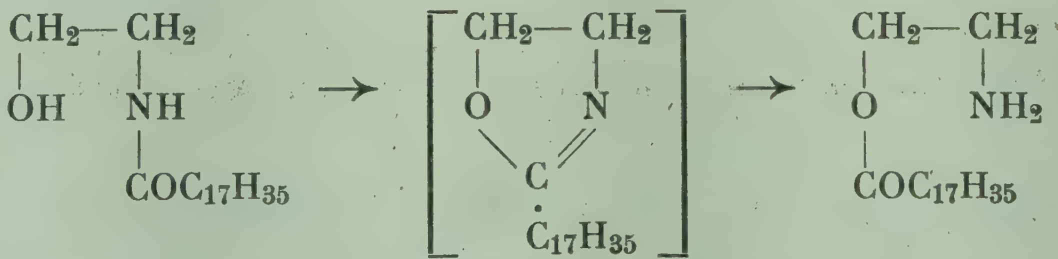
Thionyl chloride

$SOCl_2$

Acyl migration
O-Acyl from N-acyl

NAc → OAc

196.



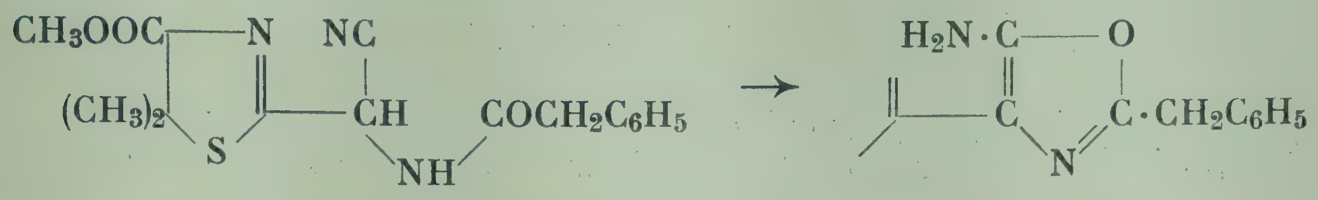
Oxazolines as intermediates. N-Stearoylethanolamine warmed at 50° with 1.25 mole $SOCl_2$ for ca. 1 hr., $SOCl_2$ distilled off in vacuo, the residue dissolved in water, and heated 0.5 hr. on a water bath → O-stearoylethanolamine (isolated as hydrochloride). Y: ca. 100%. P. Desnuelle, M. Naudet, and E. Sambuc, Bl. *1949*, 650.

Hydrochloric acid *HCl*

s. *1*, 154; s. a. L. H. Welsh, Am. Soc. *71*, 3500 (1949); H. Bretschneider et. al., M. *81*, 31 (1950)

Oxazoles from α-acylaminonitriles ○

197.



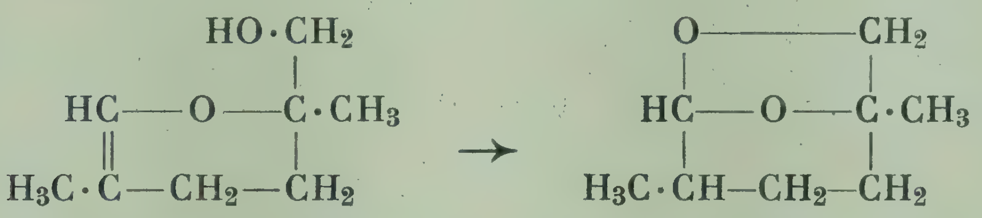
19.8 gm. methyl 5,5-dimethyl-2-[(phenylacetylamino)cyanomethyl]-thiazoline-4-carboxylate in ethyl acetate and ether containing HCl allowed to stand for 20 hrs. → 21.3 gm. 5-amino-2-benzyl-4-(4-carbomethoxy-5,5-dimethyl-2-thiazolin-2-yl)oxazole hydrochloride.—This isomerization can be reversed with bases. F. e. s. A. H. Cook, G. Harris, and A. L. Levy, Soc. *1949*, 3227.

Carbon/Carbon Type OC∩CC

Without additional reagents *w.a.r.*

m-Dioxane ring ○

198.

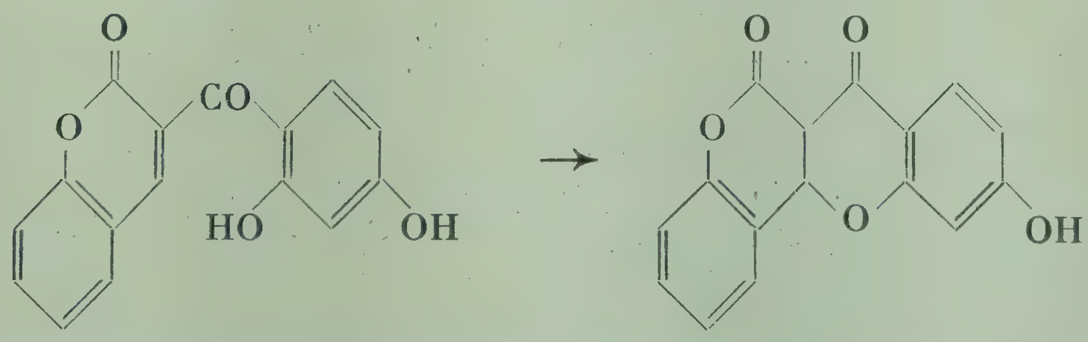


3,4-Dihydro-2,5-dimethyl-2H-pyran-2-methanol refluxed 90 min. until the boiling point has decreased to a constant value → 1,4-dimethyl-6,8-dioxabicyclo[3.2.1]octane. Y: 86%. G. G. Stoner and J. S. McNulty, Am. Soc. *72*, 1531 (1950).

Acetic acid *CH_3COOH*

Chromono(3′,2′,3,4)coumarin ring

199.

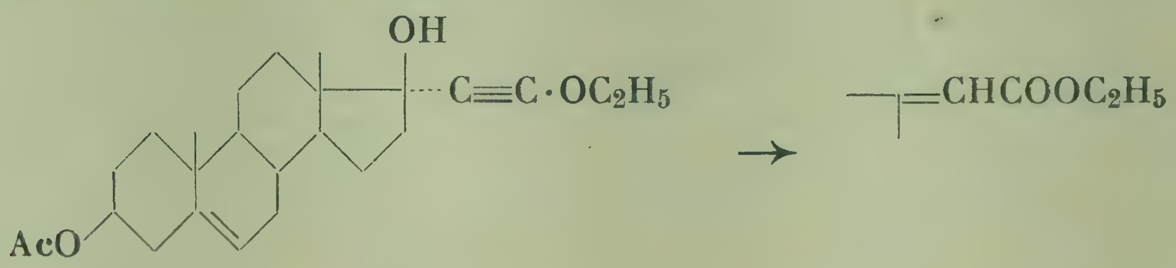


2′,4′-Dihydroxy-3-benzoylcoumarin dissolved in boiling acetic acid, and allowed to cool → 7′-hydroxy-3,4-dihydrochromanono(3′,2′,3,4)-coumarin. Y: almost 100%. F. e. s. G. Parker and A. Robertson, Soc. *1950*, 1121.

Sulfuric acid *H_2SO_4*

α,β-Ethylenecarboxylic acid esters from alkoxyacetylenealcohols ←

200.



A soln. of 300 mg. Δ^5-3β-acetoxy-17β-hydroxy-17α-ethoxyethinylandrostene in dioxane shaken 25 min. with 10%-aq.-H_2SO_4 at room temp. → 210 mg. ethyl $\Delta^{5,17(20)}$-3β-acetoxypregnadiene-21-carboxylate. H. Heusser, K. Eichenberger, and P. A. Plattner, Helv. *33,* 1088 (1950); s. a. A. Caliezi and H. Schinz, Helv. *33,* 1129 (1950).

Exchange

Hydrogen ↑ OC ⇅ H

Sodium polysulfide *Na_2S_x*

Aminoaldehydes from nitrohydrocarbons ←

s. *1,* 162; s. a. E. Campaigne, W. M. Budde, and G. F. Schaeffer, Org. Synth. *31,* 6 (1951)

Nitric acid/sodium nitrite *$HNO_3/NaNO_2$*

Carboxylic acids from alcohols $CH_2O \rightarrow COOH$

s. *6,* 170

Selenium dioxide *SeO_2*

Ketones from hydrocarbons $CH_2 \rightarrow CO$

s. *1,* 164; *2,* 186; s. a. A. G. Caldwell, F. C. Copp, and L. P. Walls, Soc. *1950,* 2698

α-Diketones from ketones $COCH_2 \rightarrow COCO$

s. *4,* 190; s. a. W. van der Haar, R. C. Voter, and C. V. Banks, J. Org. Chem. *14,* 836 (1949)

Chromic acid *CrO_3*

Carboxylic acids from alcohols $CH_2OH \rightarrow COOH$

s. *6,* 233

Hydrobromic acid *HBr*

Oxidation of hydrocarbons ←

Ketones and hydroperoxides from hydrocarbons

01.

$$CH_3CH_2CH_3 \rightarrow CH_3COCH_3$$

$$(CH_3)_3CH \rightarrow (CH)_3C\cdot OOH$$

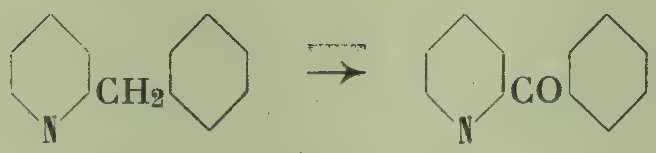
The gas phase O_2-oxidation of the lower hydrocarbons is greatly modified by the presence of HBr. Straight-chain paraffins are converted mainly to ketones, and branched-chain compounds to stable peroxides. The character of the product is determined principally by the most reactive C-H linkage. The reactivity of this linkage increases markedly in the order—primary, secondary, and tertiary. The oxidation is accompanied by a low degree of C-C bond scission, the operating temp. is low, and the conversions and yields are high.—Propane at 189° → acetone. Y: 71.6%.—Isobutane at 163° → tert-butyl hydroperoxide. Y: 69.5%. F. e. s. F. F. Rust, W. E. Vaughan et al., Ind. Eng. Chem. *41*, 2595-2612 (1949).

Potassium permanganate *$KMnO_4$*

Ketones from hydrocarbons

$CH_2 \rightarrow CO$

02.

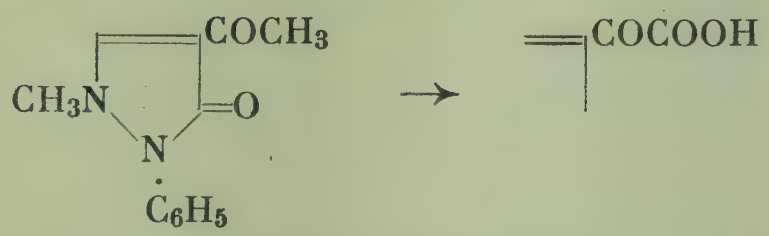


$KMnO_4$ added in portions at 70° to a stirred aq. suspension of 2-benzylpyridine, then the temp. raised to 100° until all the $KMnO_4$ has reacted → 2-benzoylpyridine. Y: 86%. E. H. Huntress and H. C. Walter, Am. Soc. *70*, 3702 (1948); method, see K. E. Crook and S. M. McElvain, Am. Soc. *52*, 4006 (1930); s. a. K. Schofield, Soc. *1949*, 2408.

α-Ketocarboxylic acids from methyl ketones

$COCH_3 \rightarrow COCOOH$

03.



A satd. soln. of $KMnO_4$ slowly added at 40° to an aq. soln. of 1-phenyl-2-methyl-4-acetyl-5-pyrazolone and KOH, and worked up after the color has disappeared → 1-phenyl-2-methyl-5-pyrazolone-4-glyoxylic acid. Y: 80%. F. e. s. K. Bodendorf and A. Popelak, A. *566*, 84 (1950).

Carboxylic acid amides from amines

$CH_2NR_2 \rightarrow CONR_2$

s. *2*, 190; s. a. Soc. *1951*, 303

Via intermediates *v.i.*

Carboxylic acids from alcohols via aldehydes $CH_2OH \rightarrow COOH$

s. 6, 292

Oxygen ↑ OC ⇅ O

Without additional reagents *w.a.r.*

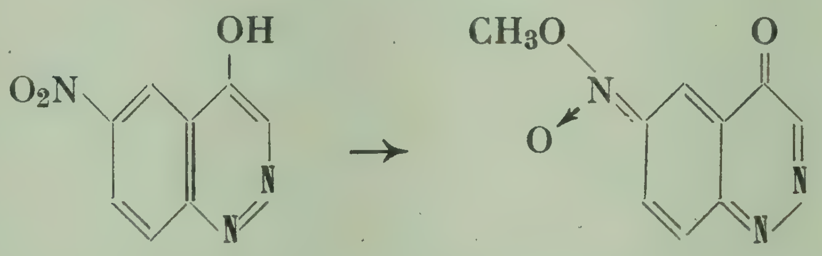
Carboxylic acid esters from carboxylic acids $COOH \rightarrow COOR$

s. *5*, 166; under a slight vacuum s. J. Colonge and P. Stuchlik, Bl. *1950*, 586; azeotropic removal of the water formed s. E. E. Burgoyne and F. E. Condon, Am. Soc. *72*, 3276 (1950); R. N. Smith and W. V. Bolliger, J. Chem. Education *27*, 369 (1950)

Potassium hydroxide *KOH*

Nitronates ←

204.



A. soln. of 6-nitro-4-hydroxycinnoline in the minimum quantity of 2%-aq.-KOH treated with dimethyl sulfate at 50° with stirring, and worked up after 15 min. → methyl 4-cinnolone-6-nitronate. Y: 55%. F. e. s. J. R. Keneford et al., Soc. *1950*, 1104.

Sodium acetate *CH_3COONa*

Acetylation $OH \rightarrow OAc$

s. *2*, 193; *3*, 158; carbohydrates s. M. L. Wolfrom, W. L. Shilling, and W. W. Binkley, Am. Soc. *72*, 4544 (1950)

Diene synthesis via enolesters ←

s. *6*, 695

Potassium acetate *CH_3COOK*

Enol acetates from aldehydes $CHCHO \rightarrow C{:}CH(OAc)$

s. *6*, 214, 575

Ammonia *NH_3*

6-Alkoxy-5,6-dihydrophenanthridines $OH \rightarrow OR$

s. *6*, 820

Pyridine *C_5H_5N*

Propionates OH → OAc

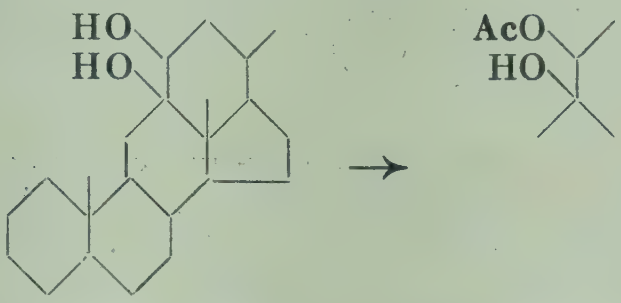
s. *2,* 198; of carbohydrates s. V. Deulofeu and F. Giménez, J. Org. Chem. *15,* 460 (1950)

Unsatd. esters of sucrose OH → OCOCH : CHCH₃

05. Crotonic anhydride added slowly with rapid stirring at 70-75° to a mixture of sucrose and pyridine, heated 5 hrs. at 80-90°, and left overnight at room temp. → octacrotonylsucrose. Y: 95%. F. e., also with carboxylic acid chlorides, s. M. Zief, Am. Soc. *72,* 1137 (1950).

Selective acylation ←

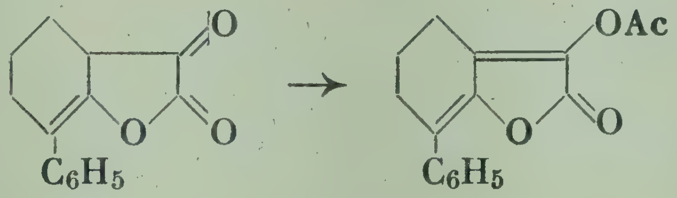
06.



Acetic anhydride added to a soln. of 12,23-dihydroxydehydronorcholane in pyridine, and allowed to stand 24 hrs. at room temp. → 23-acetoxy-12-hydroxydehydronorcholane. Y: 90%.—Only the sec. hydroxyl group is esterified. A. Butenandt and H. Dannenberg, A. *568,* 83 (1950).

Enol esters C:CH(OAc)

07.



Acetic anhydride added to a soln. of 0.5 gm. 2-hydroxy-3-phenyl-2-cyclohexeneglyoxylic acid γ-lactone (prepn. s. 746) in pyridine, and refluxed 3 min. → 0.52 gm. enol acetate. F. e. s. W. E. Bachmann, G. I. Fujimoto, and L. B. Wick, Am. Soc. *72,* 1995 (1950); s. a. R. Kuhn and K. Dury, A. *571,* 44 (1950).

Cupric acetate *$(CH_3COO)_2Cu$*

Reactions with isopropenyl acetate ←
Acetylation, enol acetates
Acetylamines

08. $CH_3CH{=}CHCHO$ → $CH_2{=}CHCH{=}CHOCOCH_3$

$+ \ CH_2{=}C(CH_3)OCOCH_3$

$(CH_3)_2CHCH_2NH_2$ → $(CH_3)_2CHCH_2NHCOCH_3$

Isopropenyl acetate is an excellent acetylating agent, which is decomposed into the original components, ketene and acetone, by heating in the presence of acid catalysts. It is superior to ketene and acetic anhydride for enol acetylation and it reacts with all enolizable carbonyl compounds. It is particularly useful for acetylation under mild conditions.—E: Crotonaldehyde added to isopropenyl acetate containing some p-toluenesulfonic acid and a little Cu-acetate over a period of 2-3 hrs., while the acetone formed is distilled off → 1-acetoxy-1,3-butadiene. Y: 90%.—Similarly: Isobutylamine added to isopropenyl acetate → N-isobutylacetamide. Y: 94%. F. e. and reactions s. H. J. Hagemeyer, Jr., and D. C. Hull, Ind. Eng. Chem. *41*, 2920 (1949).

Boron fluoride *BF_3*

Acylation OH → OAc

s. *1*, 177; *2*, 202; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. *71*, 3938 (1949); T. W. Campbell and G. M. Coppinger, Am. Soc. *73*, 2708 (1951).

Carboxylic acid esters from carboxylic acids COOH → COOR

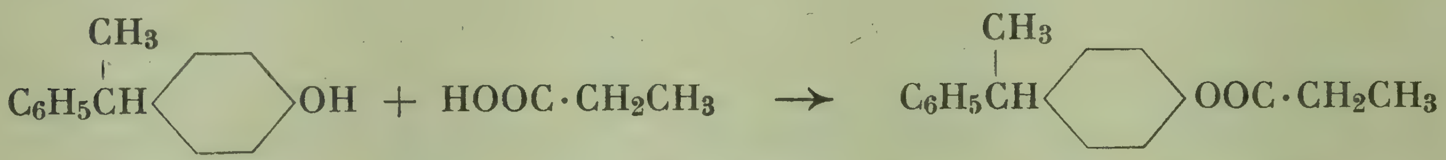
209. BF_3-ethyl ether complex added slowly below 40° to a suspension of 4-amino-2-hydroxybenzoic acid in anhydrous isopropanol, and allowed to stand at room temp. for several days → isopropyl 4-amino-2-hydroxybenzoate. Y: 75%.—Other methods gave very low yields, the primary product being m-aminophenol. F. e. s. J. J. Schaefer and L. Doub, Am. Soc. *71*, 3564 (1949).

Bauxite *Al_2O_3*

s. *6*, 420

Acetic anhydride *$(CH_3CO)_2O$*

210.



A mixture of p-(α-phenylethyl)phenol, propionic acid, and acetic anhydride refluxed ca. 0.5 hr., then the acetic acid formed distilled off → p-(α-phenylethyl)phenyl propionate. Y: 93%. F. e. s. K. C. Frisch, J. Org. Chem. *15*, 587 (1950).

Trifluoroacetic anhydride *$(CF_3CO)_2O$*

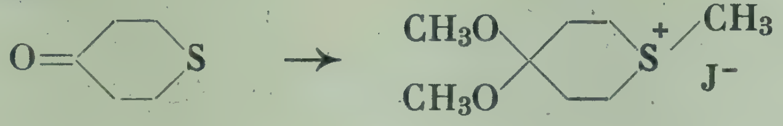
211. **Acylation of hydroxy compounds.** Esters can be produced from alcohols and phenols by treatment with carboxylic acids in the presence of trifluoroacetic anhydride. The method can be used to esterify carboxylic acids in both the aliphatic and the aromatic series. In many cases the reaction proceeds spontaneously and is essentially complete within a few minutes. The general conditions of the reaction are relatively mild and enable, for example, acyl derivatives to be prepared

in good yield from acid-labile glycosides. The method is particularly convenient for the acylation of polysaccharides and also for the production of poly-esters.—E: Trifluoroacetic anhydride introduced into a mixture of D-mannitol and glacial acetic acid, and allowed to cool slowly → D-mannitol hexaacetate. Y: 80%.—Palmitic acid and trifluoroacetic anhydride mixed, kept at room temp. for 30 min., β-naphthol added, and worked up after 45 min. at room temp. and 5 min. at 50° → β-naphthyl palmitate. Y: 85%. F. e. s. E. J. Bourne et al., Soc. *1949*, 2976.

Methyl iodide *CH_3I*

Ketals with simultaneous formation of sulfonium salts ←

212.



Thiacyclohexan-4-one in refluxing methanol treated with methyl iodide, and refluxing continued for 2.5 hrs. → 4,4-dimethoxythiacyclohexane methiodide. Y: 78%.—The ketomethiodide can be obtained at room temp. F. ketals s. H. M. E. Cardwell, Soc. *1950*, 1059.

Ammonium nitrate *NH_4NO_3*

α,β-Ethyleneacetals from α,β-ethylenealdehydes CHO → CH(OR)₂

s. *6*, 220

Phosphorus pentoxide *P_2O_5*

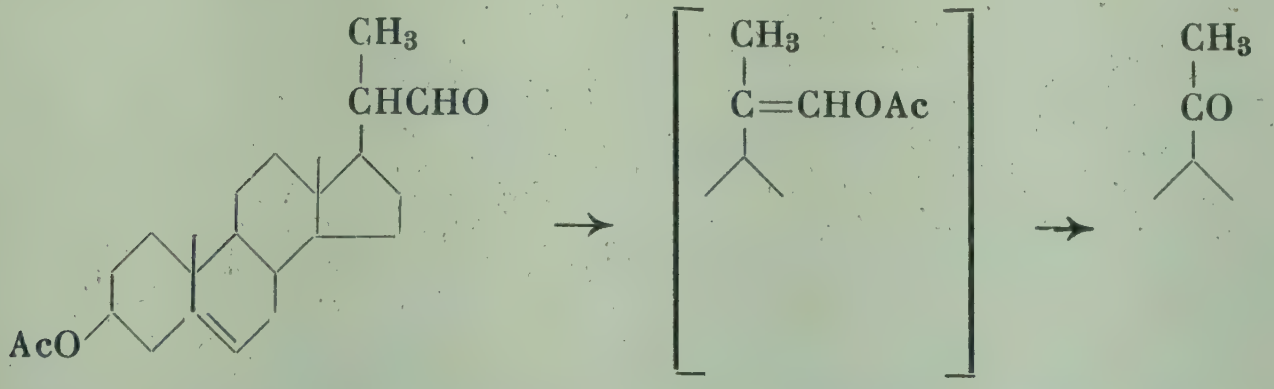
Carboxylic acid esters from carboxylic acids COOH → COOR

213. Methacrylic acid (prepn. s. 292) refluxed 4 hrs. with excess methanol in the presence of P_2O_5 → methyl methacrylate. Y: ca. 100%. J. M. Church and L. Lynn, Ind. Eng. Chem. *42*, 768 (1950).

Ozone *O_3*

Ketones from aldehydes via enolesters ←
Degradation with loss of 1 C-atom

214.

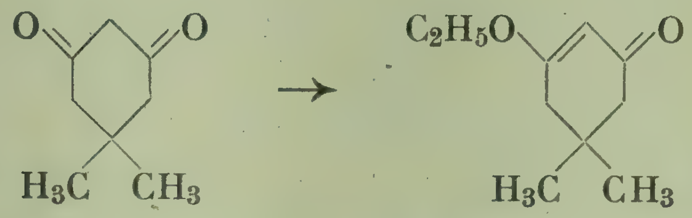


A mixture of 3β-acetoxybisnor-5-cholenaldehyde, acetic anhydride, and freshly fused Na-acetate refluxed 8 hrs. under N_2, evaporated to dryness under reduced pressure, redissolved in chloroform, the insoluble Na-acetate removed by filtration, ozonized with ice-cooling for 22 min., chloroform removed in vacuo, and the ozonide decomposed with Zn-dust and glacial acetic acid in the presence of ether → 5-pregnene-3β-ol-20-one acetate. Y: 57%. F. e. s. F. W. Heyl and M. E. Herr, Am. Soc. *72*, 2617 (1950).

p-Toluenesulfonic acid *TsOH*

Enolethers C:C(OR)

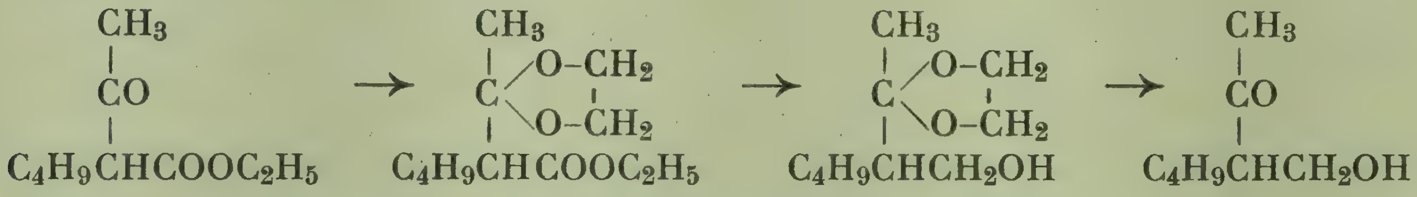
215.



A mixture of methone, abs. ethanol, benzene, and a small amount of p-toluenesulfonic acid refluxed under a continuous water separator until no more water was formed → 5,5-dimethyl-3-ethoxy-2-cyclohexenone. Y: 83%. F. e. s. R. L. Frank and H. K. Hall, Jr., Am. Soc. *72*, 1645 (1950).

β-Hydroxyketones from β-ketocarboxylic acid esters ←
Protection of the carbonyl group
Alkylene acetals

216.



$$\begin{array}{c} CH_3 \\ | \\ CO \\ | \\ C_4H_9CHCOOC_2H_5 \end{array} \rightarrow \begin{array}{l} CH_3 \\ |\diagup O\text{-}CH_2 \\ C \qquad\;\; | \\ |\diagdown O\text{-}CH_2 \\ C_4H_9CHCOOC_2H_5 \end{array} \rightarrow \begin{array}{l} CH_3 \\ |\diagup O\text{-}CH_2 \\ C \qquad\;\; | \\ |\diagdown O\text{-}CH_2 \\ C_4H_9CHCH_2OH \end{array} \rightarrow \begin{array}{c} CH_3 \\ | \\ CO \\ | \\ C_4H_9CHCH_2OH \end{array}$$

Ethyl α-butylacetoacetate, ethylene glycol, benzene, and a trace of p-toluenesulfonic acid refluxed 10 hrs. with separation of the water formed → ethyl α-butylacetoacetate ethyleneketal (Y: 84%) reduced with Na in abs. alcohol at an oil bath temp. of ca. 160° → 2-butyl-2-acetylethanol ethylene ketal (Y: 77%) heated 1 hr. with water-alcohol and a drop of concd. HCl on a water bath → 2-butyl-2-acetylethanol (Y: 89%).—Alkylene acetals are more stable than dialkyl acetals and can easily be prepared by the above method, which is not limited to enolizable carbonyl groups. F. e. s. L. Willimann and H. Schinz, Helv. *32*, 2151 (1949); preparation of steroid ketals with toluene in place of benzene, and hydrolysis by p-toluenesulfonic acid s. C. A. Grob, W. Jundt, and H. Wicki, Helv. *32*, 2427 (1949).

Acetylation of alcohols by azeotropic distillation OH → OAc

217. $ClCH_2CH_2CH_2OH + HOOC\cdot CH_3 \rightarrow ClCH_2CH_2CH_2OOC\cdot CH_3$

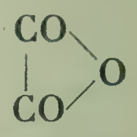
A mixture of trimethylene chlorohydrin, glacial acetic acid, benzene, and p-toluenesulfonic acid monohydrate refluxed for 7-9 hrs. with distillation of the benzene-water azeotrope → γ-chloropropyl acetate. Y: 93-95%. C. F. H. Allen and F. W. Spangler, Org. Synth. *29*, 33 (1949).

Sulfuric acid *H_2SO_4*

Ethers from alcohols ROH → ROR′

s. *4*, 201; s. a. R. C. Fuson and H. L. Jackson, Am. Soc. *72*, 351 (1950)

Ethylidene derivatives of carbohydrates

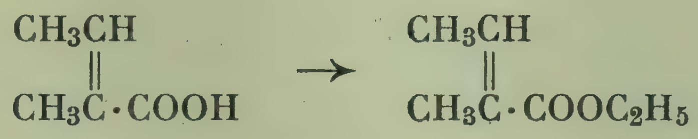


s. *2*, 205; s. a. R. C. Hockett, D. V. Collins, and A. Scattergood, Am. Soc. *73*, 599 (1950)

Carboxylic acid esters from carboxylic acids COOH → COOR

Azeotropic distillation

218.



$$\begin{array}{l} CH_3CH \\ \quad\; \| \\ CH_3C\cdot COOH \end{array} \rightarrow \begin{array}{l} CH_3CH \\ \quad\; \| \\ CH_3C\cdot COOC_2H_5 \end{array}$$

A mixture of tiglic acid, abs. ethanol, benzene, and some concd. H_2SO_4 refluxed 24 hrs. in a Soxhlet extraction apparatus, the thimble of which contains CaC_2 → ethyl tiglate. Y: 74-80%. R. E. Buckles and G. V. Mock, J. Org. Chem. *15*, 680 (1950).

with $MgSO_4$ in the thimble s. *3*, 168; s. a. W. Baker and W. D. Ollis, Soc. *1951*, 556.

Perchloric acid *$HClO_4$*

Acetylation OH → OAc

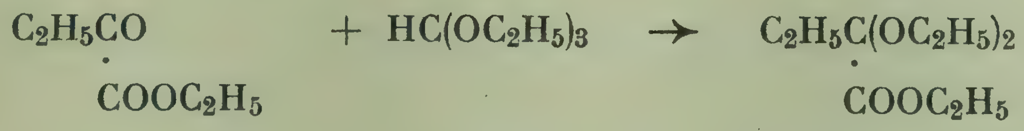
s. *3*, 171; s. a. H. Burton and P. F. G. Praill, Soc. *1950*, 1203

of carbohydrates
Acetobromosugars
s. *6*, 582

Hydrochloric acid *HCl*

Acetals with orthoformate CO → $C(OR)_2$

219.



$$\begin{array}{l} C_2H_5CO \\ \qquad\cdot COOC_2H_5 \end{array} + HC(OC_2H_5)_3 \rightarrow \begin{array}{l} C_2H_5C(OC_2H_5)_2 \\ \qquad\cdot COOC_2H_5 \end{array}$$

Ethyl α-ketobutyrate, orthoformate, and abs. alc. HCl allowed to stand overnight in a closed flask → ethyl α-ketobutyrate diethylketal. Y: 89%. F. e. s. E. Vogel and H. Schinz, Helv. *33*, 116 (1950); method, s. Claisen, B. *29*, 1005 (1896); *40*, 3903 (1907).

α,β-Ethyleneacetals and β-alkoxyacetals from α,β-ethylenealdehydes ←

220.

$$\begin{tikzcd}
 & CH_2{=}CHCHO \arrow[dl] \arrow[dr] & \\
CH_2{=}CHCH(OC_2H_5)_2 & & C_2H_5OCH_2CH_2CH(OC_2H_5)_2
\end{tikzcd}$$

A warm soln. of NH_4-nitrate in dry alcohol added to a mixture of acrolein and ethyl orthoformate, then refluxed 8–10 min. → acrolein diethyl acetal. Y: 73%. H. O. L. Fischer and E. Baer, Helv. *18,* 514 (1935).

A mixture of acrolein, ethyl orthosilicate, and abs. ethanol containing anhydrous HCl allowed to stand at room temp. for 2 weeks → β-ethoxypropionaldehyde diethyl acetal. Y: 76%. C.E. Feazel and W.G. Berl, Am. Soc. *72,* 2278 (1950); s. a. F. Krausz, Ann. chim. [12] *4,* 811 (1949).

Dehydration with simultaneous esterification ←

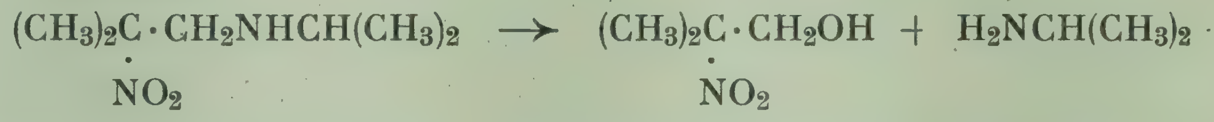
s. *6,* 689; cf. L. F. Fieser and S. Rajagopalan, Am. Soc. *72,* 5530 (1950)

Nitrogen ↑ OC ⇅ N

Without additional reagents *w.a.r.*

Cleavage of nitramines ←
Steric hindrance

221.

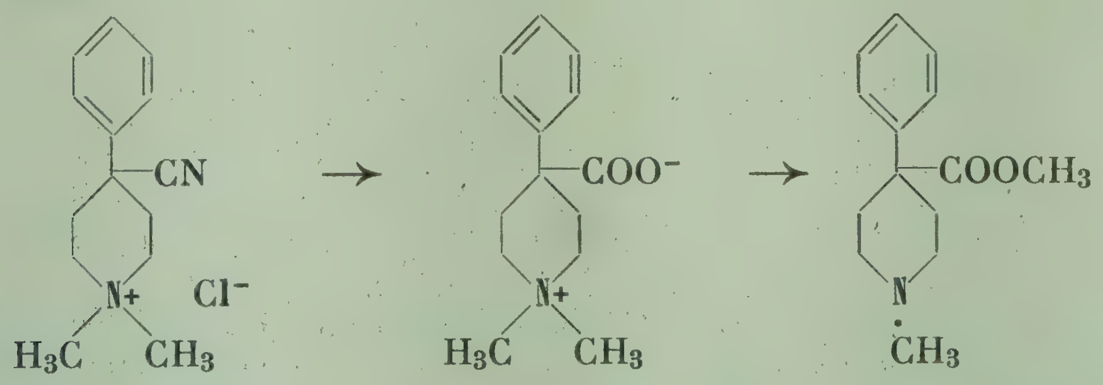


$$(CH_3)_2\underset{NO_2}{C}\cdot CH_2NHCH(CH_3)_2 \rightarrow (CH_3)_2\underset{NO_2}{C}\cdot CH_2OH + H_2NCH(CH_3)_2$$

Certain sterically hindered nitramines exhibit marked instability in the presence of water.—E: N-(2-Nitroisobutyl)isopropylamine distilled with water → isopropylamine (conversion 83%) and 2-nitro-2-methyl-1-propanol (conversion 62%). F. e. s. M. Senkus, Am. Soc. *72,* 2069 (1950).

Aminocarboxylic acid esters from quaternary cyanoammonium salts via betaines ←

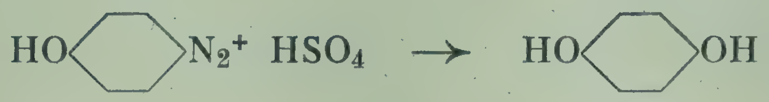
222.



1,1-Dimethyl-4-phenyl-4-cyanopiperidinium chloride refluxed 3.5 hrs. with 1 mole of aq. NaOH → 1,1-dimethyl-1-hydroxy-4-phenylpiperidinium-4-carboxylic acid betaine heated in vacuo → methyl 1-methyl-4-phenylpiperidine-4-carboxylate. Y: 81.5%.—Cyanopiperidinium salts, like the above mentioned, are quite reactive, particularly their cyano group. F. e. s. H. Kägi and K. Miescher, Helv. *32*, 2489 (1949).

Phenols from diazonium salts ←

223.



A cooled aq. soln. of p-hydroxybenzenediazonium hydrogen sulfate irradiated with a mercury lamp → hydroquinone. Y: 88%.—Side reactions are largely avoided by irradiation of a very dilute soln. at a temp. slightly above 0° and by using a high light intensity. F. e. s. J. de Jonge and R. Dijkstra, R. *68*, 426 (1949).

Sodium hydroxide *NaOH*

Carboxylic acids from barbituric acids ↺

s. *6*, 290

α-Aminocarboxylic acids from hydantoins

s. *6*, 761/2

Potassium hydroxide *KOH*

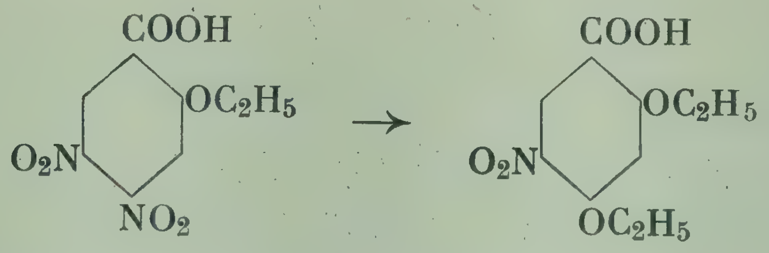
Carboxylic acids from cyanocarboxylic acid esters ←

s. *6*, 700

Potassium hydroxide/alcohol

Replacement of mobile nitro groups by alkoxyl $NO_2 \rightarrow OR$

224.



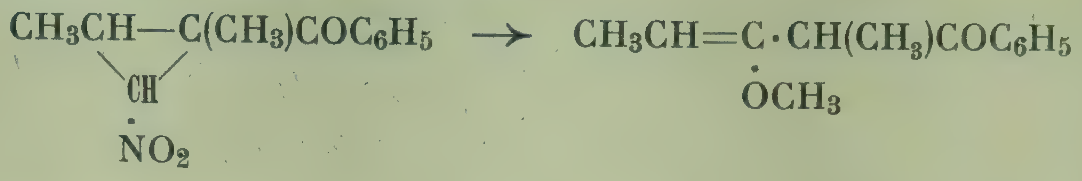
A soln. of 4,5-dinitro-2-ethoxybenzoic acid in abs. alcohol added to a soln. of KOH in abs. alcohol, and warmed at 50° for 0.5 hr. → 5-nitro-2,4-diethoxybenzoic acid. Y: 82%. H. Goldstein and R. Brochon, Helv. *32*, 2334 (1949).

Sodium/alcohol *NaOR*

C

Nitrocyclopropane ring opening

225.



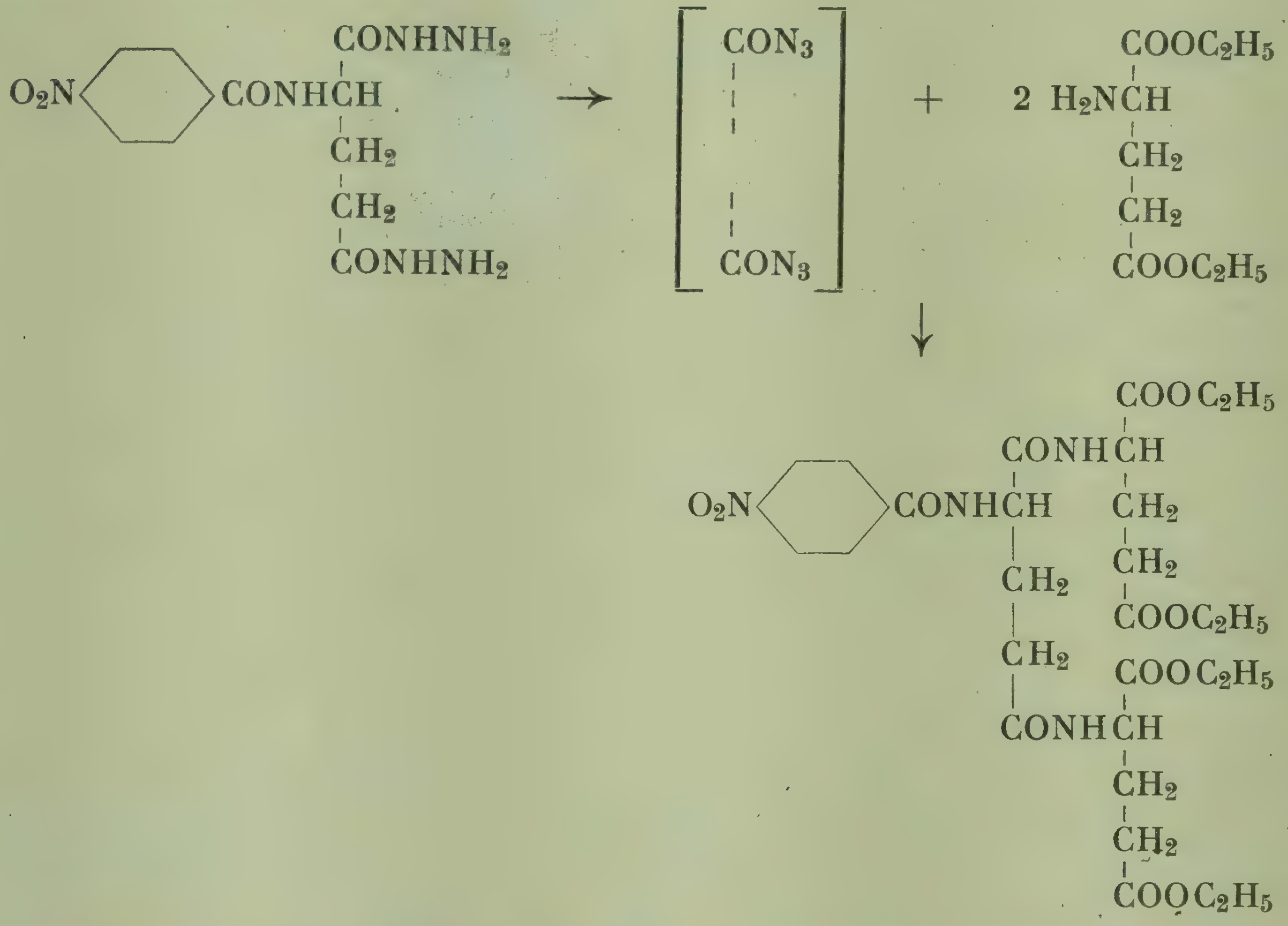
1,3-Dimethyl-2-nitro-1-cyclopropyl phenyl ketone added with stirring to a soln. of Na in dry methanol, and stirring continued for 2.5 hrs. → β-methoxy-α-methyl-β-pentenophenone. Y: 77%. F. e. s. L. I. Smith and V. A. Engelhardt, Am. Soc. *71*, 2671 (1949).

Sodium hydrogen carbonate *NaHCO₃*

Subst. carboxylic acid amides from carboxylic acid hydrazides via carboxylic acid azides

$CONHNH_2 \rightarrow CONHR$

226.



A cold aq. soln. of $NaNO_2$ added with vigorous stirring below 5° during 25 min. to a mixture of p-nitrobenzoylglutamic acid dihydrazide, aq. HCl, and ethyl acetate, stirring continued for 40 min., the soln. in ethyl acetate of the diazide obtained added to a well stirred soln. of diethylglutamate hydrochloride in a mixture of water and $NaHCO_3$, and stirring continued at room temp. for ca. 5 hrs. → p-nitrobenzoyl-α,γ-glutamyldiglutamic acid tetra ethyl ester. Y: 61%. F. e. s. J. H. Mowat et al., Am. Soc. *71*, 2308, 2304, 2310 (1949); cf. H. Adkins, R. M. Ross, and D. C. Schroeder, Am. Soc. *72*, 5401 (1950).

Sodium acetate *CH_3COONa*

Carboxylic acids from prim. nitro compounds $CH_2NO_2 \rightarrow COOH$

227. $C_6H_5CH_2NO_2 \rightarrow C_6H_5COOH + AcO \cdot N(Ac)_2$

Na-acetate added to a soln. of phenylnitromethane in acetic anhydride, and refluxed 30 min. → triacetylhydroxylamine (startg. m. f. 387) (Y: 56%) and benzoic acid (Y: 84%). F. e. s. T. Urbanski, Soc. *1949*, 3374.

Sodium nitrite *$NaNO_2$*

Cleavage of nucleosides
with subsequent replacement of
amino groups by hydroxyl $NH_2 \rightarrow OH$

s. *6*, 44

Ammonia *NH_3*

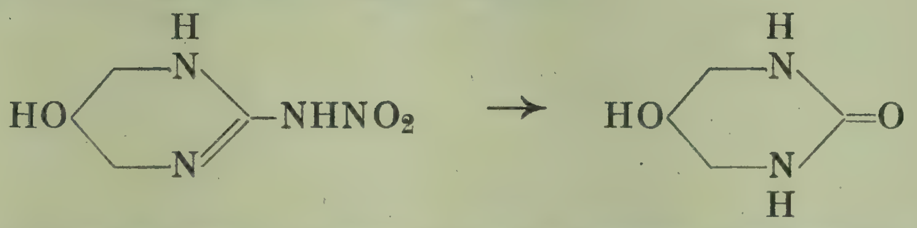
Carboxylic acids from barbituric acids

228. 5-Phenyl-5-ethylbarbituric acid hydrolized with 10% aq. NH_3 → phenyl-ethylacetic acid. Y: 80%. B. Samdahl and B. Berg, Bl. *1949*, 461; C. r. *228*, 1894 (1949).

Benzylamine *$C_6H_5CH_2NH_2$*

Cyclic ureas from cyclic nitroguanidines ←

229.



2-Nitramino-5-hydroxy-1,3-diaza-2-cyclohexene refluxed 14 hrs. in water containing a small quantity of benzylamine → 4-hydroxy-2,6-diaza-1-cyclohexanone. Y: 98%. F. e. s. A. F. McKay, J. R. Coleman, and G. A. Grant, Am. Soc. *72*, 3205 (1950); cf. *72*, 3659.

Silver oxide *Ag_2O*

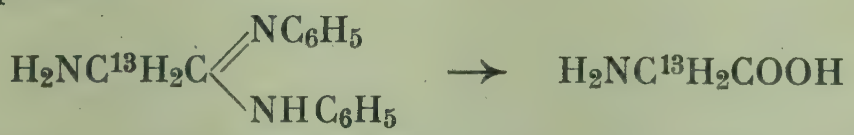
Malonic acid esters from
carboxylic acid bromides via
diazo compounds ←

s. *6*, 795

Barium hydroxide *$Ba(OH)_2$*

Carboxylic acids from nitriles
Labeled compounds $CN \rightarrow COOH$

230.



$$H_2NC^{13}H_2C{\Large\langle}\begin{matrix}NC_6H_5\\NHC_6H_5\end{matrix} \rightarrow H_2NC^{13}H_2COOH$$

Methylene-labeled (N,N-diphenyl)aminoacetamidine (prepn. 74) refluxed with a 10% soln. of $Ba(OH)_2$ at an oil bath temp. of 130° for 1 hr. → methylene-labeled glycine. Y: almost 100%. G. Ehrensvärd and R. Stjernholm, Acta Chem. Scand. *3*, 971 (1949).

Pyruvic acid $CH_3COCOOH$

Cleavage of hydrazones $C:N'NHR \rightarrow C:O$

s. *6*, 290, 891

Cleavage of semicarbazones $C:N'NHCONH_2 \rightarrow C:O$

s. *6*, 891

Acetic anhydride $(CH_3CO)_2O$

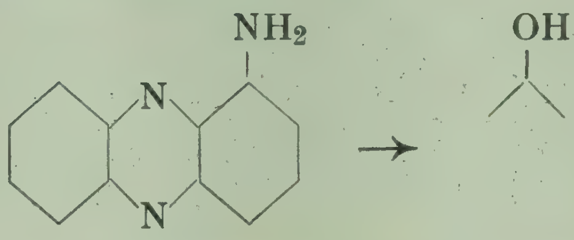
Acoxy compounds from tert. amines $NR_2 \rightarrow OAc$

s. *6*, 731; s. a. E. L. Eliel, Am. Soc. *73*, 43 (1951)

Phosphoric acid H_3PO_4

Replacement of amino groups by hydroxyl $NH_2 \rightarrow OH$

231.



1-Aminophenazine heated with 3 *N* H_3PO_4 at 150-160° in a sealed tube for 36 hrs. → 1-hydroxyphenazine. Y: 53%.—Refluxing in an open vessel is almost without effect. B. Hegedüs, Helv. *33*, 766 (1950).

Sulfur dioxide SO_2

Replacement of amino groups by hydroxyl $NH_2 \rightarrow OH$
Modified Bucherer reaction

s. *4*, 224; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. *73*, 1414 (1951)

Sulfuric acid H_2SO_4

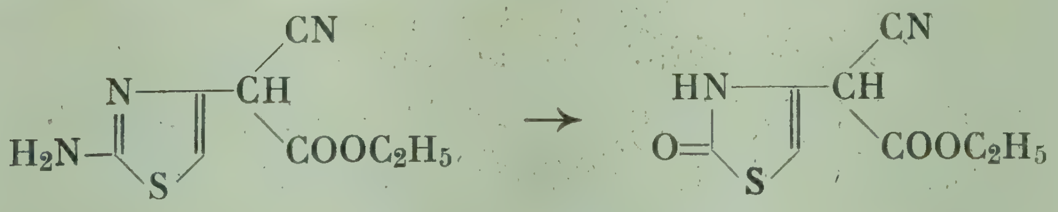
Carboxylic acid esters from nitriles $CN \rightarrow COOR$

s. *3*, 196; s. a. H. F. Piepenbrink, A. *572*, 83 (1951)

Sulfuric acid/alcohol H_2SO_4/C_2H_5OH

2-Thiazolones from 2-aminothiazoles ←

232.

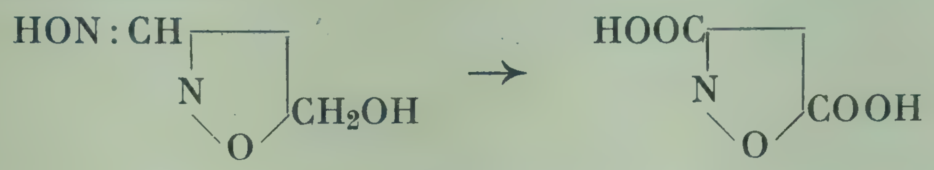


A mixture of ethyl (2-amino-4-thiazolyl)cyanoacetate, concd. H_2SO_4, and abs. alcohol heated on a water bath for ca. 2-3 hrs. until the ester is dissolved → ethyl (thiazol-2-on-4-yl)cyanoacetate. Y: ca. 80%. H. Beyer and H. Höhn, B. *83*, 14 (1950).

Chromic acid *CrO_3*

Carboxylic acids from aldoximes and alcohols ←

233.

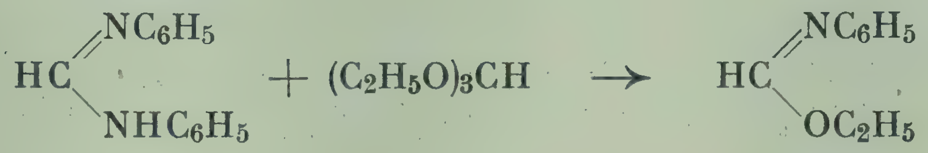


5-Hydroxymethyl-3-isoxazolecarboxaldehyde oxime and a soln. of $K_2Cr_2O_7$ in 10%-H_2SO_4 refluxed ca. 1 hr. → 3,5-isoxazoledicarboxylic acid. Y: almost 100%. F. e. s. A. Quilico and G. Stagno D'Alcontres, G. *79*, 654 (1949).

Hydrochloride ←

Iminoesters from amidines and orthoformic acid esters ←

234.



$$HC\begin{matrix}\nearrow NC_6H_5\\ \searrow NHC_6H_5\end{matrix} + (C_2H_5O)_3CH \rightarrow HC\begin{matrix}\nearrow NC_6H_5\\ \searrow OC_2H_5\end{matrix}$$

A mixture of N,N′-diphenylformamidine, ethyl orthoformate, and aniline hydrochloride refluxed 1 hr., distilled for 15 min., anhydrous K-carbonate added, shaken, and allowed to stand for 2 hrs. → ethyl N-phenylformimidate (startg. m. f. 808). Y: 96%. F. e. s. R. M. Roberts, Am. Soc. *71*, 3848 (1949).

Hydrochloric acid *HCl*

Oxo compounds from imines $C{:}NH \rightarrow C{:}O$

s. 6, 483

Isatins from 2-iminoisatins

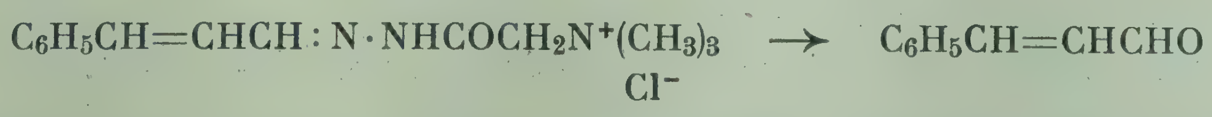
s. *6*, 871

Cleavage of azomethines $C{:}NR \rightarrow C{:}O$

235. 2-Methyl-2-pentenylidene-isobutylamine (prepn. s. 741) refluxed in HCl with stirring for ¾ hr. → 2-methyl-2-pentenal. Y: 86%. F. e. s. A. M. Paquin, B. *82*, 316 (1949).

Aldehydes from hydrazones $CH{:}N{\cdot}NHR \rightarrow CHO$
Cleavage of Girard derivatives

236.

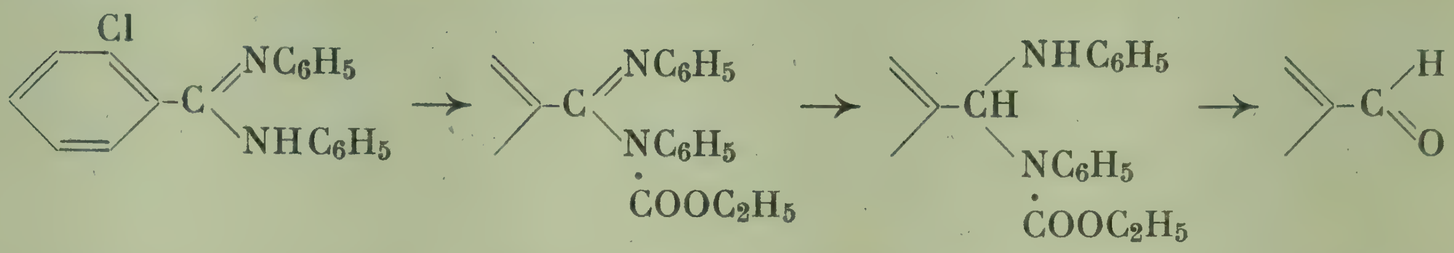


$$C_6H_5CH{=}CHCH{:}N{\cdot}NHCOCH_2\underset{Cl^-}{N^+(CH_3)_3} \rightarrow C_6H_5CH{=}CHCHO$$

Aldehyde derivatives of Girard reagents T (acethydrazide-trimethylammonium chloride) and P (acethydrazide-pyridinium chloride) are as easily hydrolyzed by 0.5-2 *N* HCl as the ketone derivatives.—E: Cinnamic aldehyde. Recovery: 90%. F. e. s. E. Lederer and G. Nachmias, Bl. *1949*, 400.

Aldehydes from amidines via 1,1-diamines N-Carbethoxyamidines Preparation of aluminum amalgam ←

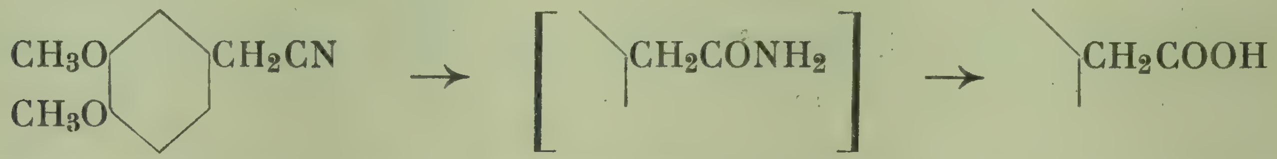
237.



4.8 gm. ethyl chloroformate slowly added with cooling to a soln. of 15 gm. N,N′-diphenyl-o-chlorobenzamidine in dry benzene containing $NaHCO_3$, and kept overnight at 0° → 8 gm. N,N′-diphenyl-N-carbethoxy-o-chlorobenzamidine, reduced with Al,Hg (prepn. given in detail in the original paper) in moist ethyl acetate or ether → N,N′-diphenyl-N-carbethoxydihydro-o-chlorobenzamidine (Y: good), 2 gm. of which hydrolyzed with concd. HCl → 0.4 gm. o-chlorobenzaldehyde.—This method can be used to convert ar. carboxylic acids into aldehydes. M. V. Shirsat and R. C. Shah, J. Indian Chem. Soc. *27*, 13 (1950).

Carboxylic acids from nitriles CN → COOH

238.

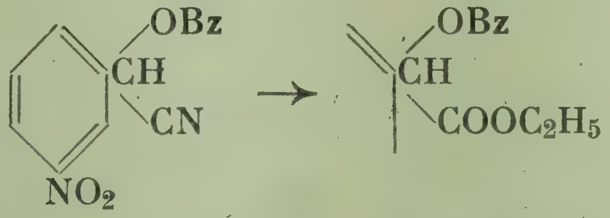


Vigorous stirring with aq. concd. HCl at low temp. converts arylacetonitriles into the corresponding amides. These amides are easily saponified to the acids by heating with dil. HCl.—E: 3,4-Dimethoxytolunitrile stirred with concd. HCl below 40° for ca. 3 hrs. until the nitrile is dissolved, warmed at 50° for 2 hrs., water added, and refluxed 7 hrs. with stirring → homoveratric acid. Y: 95%. F. e. s. W. Wenner, J. Org. Chem. *15*, 548 (1950).

Carboxylic acid esters from nitriles CN → COOR

s. *3*, 200; s. a. R. A. Cutler, A. R. Surrey, and J. B. Cloke, Am. Soc. *71*, 3375 (1949).

239.



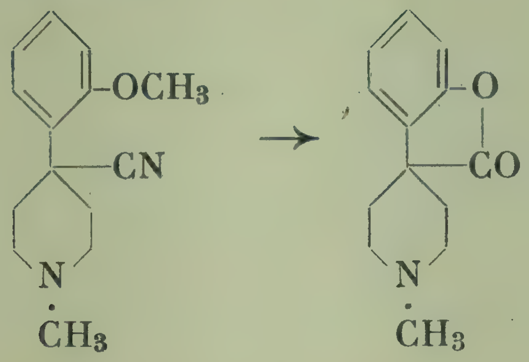
α-Acoxycarboxylic acid esters. m-Nitro-0-benzoylmandelonitrile added to a soln. of dry HCl in abs. ethanol, heated to refluxing, water added in several portions with swirling, and filtered hot after refluxing for 30 min. → ethyl m-nitro-0-benzoylmandelate (startg. m. f. 110). Y: 90%. M. W. Cronyn, J. Org. Chem. *14*, 1013 (1949).

Dicarboxylic acids from dicyanocarboxylic acid esters ←
s. *6*, 705

Hydrobromic acid *HBr*

Lactones from alkoxynitriles ○

40.

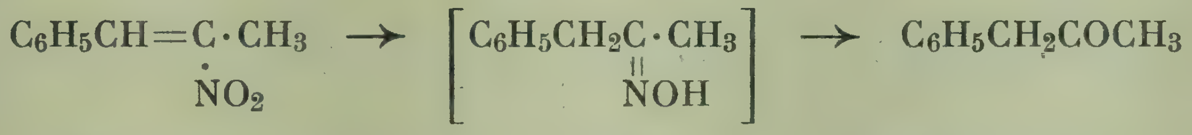


1-Methyl-4-o-methoxyphenyl-4-cyanopiperidine refluxed 6 hrs. with 10 *N* HBr → 1-methyl-4-o-hydroxyphenylpiperidine-4-carboxylic acid lactone hydrobromide (startg. m. f. 687). Y: 80%. F. e. s. H. Kägi and K. Miescher, Helv. *32*, 2489 (1949).

Iron/ferric chloride *Fe/FeCl$_3$*

Ketones from α-nitroethylene derivatives $CH:C(NO_2) \rightarrow CH_2CO$

41.



$$C_6H_5CH{=}\underset{NO_2}{C}\cdot CH_3 \longrightarrow \left[C_6H_5CH_2\underset{NOH}{\underset{\|}{C}}\cdot CH_3\right] \longrightarrow C_6H_5CH_2COCH_3$$

Concd. HCl added dropwise at a bath temp. of 85-95° over a period of 5-6 hrs. to 1-phenyl-2-nitropropene (prepn. s. 755), cast iron turnings, and a little FeCl$_3$ in water → phenylacetone. Y: 77%.—With less HCl, the ketoxime can be obtained in fair yield. F. e. s. H. B. Hass, A. G. Susie, and R. L. Heider, J. Org. Chem. *15*, 8 (1950); s. a. J. A. Pearl and D. L. Beyer, J. Org. Chem. *16*, 221 (1951).

Ferric sulfate *Fe$_2$(SO$_4$)$_3$*

Quinones from aminophenols ←
s. *1*, 173

Halogen ↑ OC ⇅ Hal

Without additional reagents *w.a.r.*

Glycosides from benzoylated halogenosugars ←
s. *5*, 192; s. a. Am. Soc. *72*, 4173 (1950).

β-Dialkylaminoethyl esters $COCl \rightarrow COOR$
s. *2*, 238; s. a. R. Fusco et al., G. *79*, 129 (1949).

Chloroformates OCOCl

s. *3*, 368; without solvent s. A. C. Farthing, Soc. *1950*, 3213

Sodium *Na*

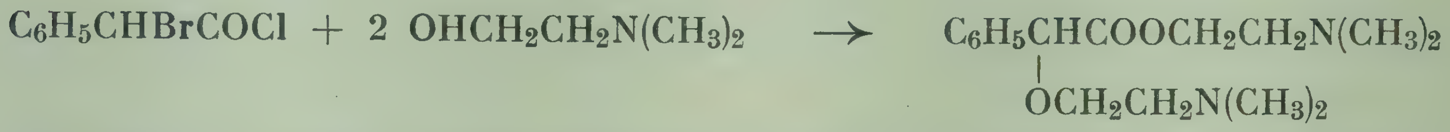
Disaccharides from monosaccharides ROR

s. *3*, 203; in air s. Soc. *1951*, 285

Potassium *K*

α-Alkoxycarboxylic acid esters from α-bromocarboxylic acid chlorides ←

242.

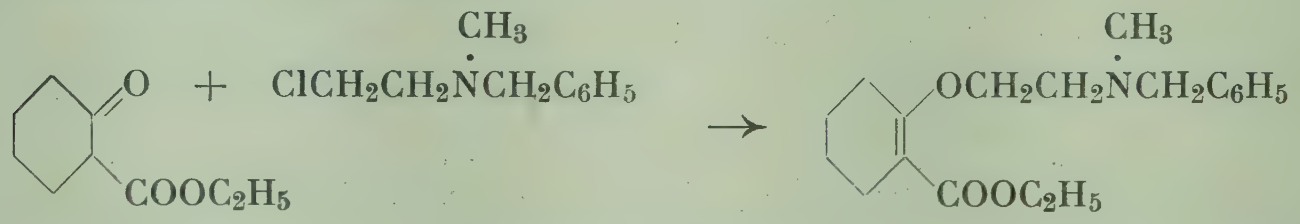


$$C_6H_5CHBrCOCl + 2\ OHCH_2CH_2N(CH_3)_2 \rightarrow \underset{\displaystyle OCH_2CH_2N(CH_3)_2}{C_6H_5CHCOOCH_2CH_2N(CH_3)_2}$$

K added to a soln. of β-dimethylaminoethanol in toluene, after reaction of all of the K a soln. of freshly distilled α-bromophenylacetyl chloride in dry toluene added dropwise with stirring, and refluxed 4-10 hrs. with continuous stirring → 2-dimethylaminoethyl α-(2-dimethylaminoethoxy)phenylacetate. Y: 77%. F. e. s. P. Truitt et al., Am. Soc. *71*. 3479 (1949).

Carbalkoxyenolethers from β-ketocarboxylic acid esters ←

243.

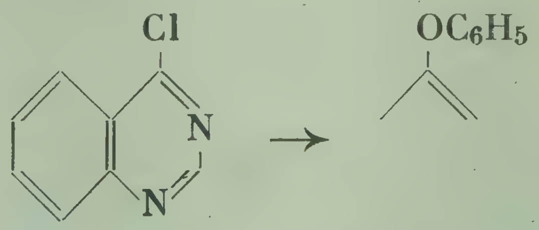


Two alkylating agents, bromoacetaldehyde diethylacetal and methylbenzyl-β-chloroethylamine, were found to O-alkylate 2-carbethoxycyclohexanone.—E: 2-Carbethoxycyclohexanone added dropwise with stirring to a suspension of K sand in toluene, refluxed ca. 20 min. until a clear soln. results, cooled to room temp., a soln. of methylbenzyl-β-chloroethylamine in toluene added, and refluxed 7 hrs. → ethyl-2-(β-methylbenzylaminoethoxy)-1-cyclohexenecarboxylate. Y: 48.4%. F. e. s. J. C. Sheehan and C. E. Mumaw, Am. Soc. *72*, 2127 (1950).

Potassium hydroxide *KOH*

Phenol ethers from halides Hal → OR

244.



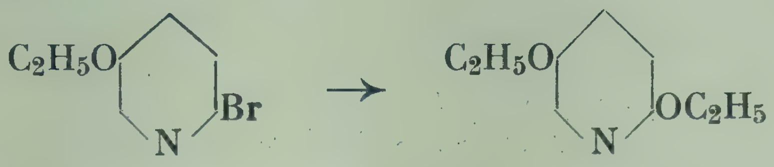
4-Chloroquinazoline added during 10 min. to a soln. of KOH in phenol at ca. 50°, and kept at this temp. for 1 hr. → 4-phenoxyquinazoline (startg. m. f. 500). Y: 90%. J. S. Morley and J. C. E. Simpson, Soc. *1949*, 1354; s. a. A. Sadykov, Ж. *19*, 143 (1949); C. A. *43*, 6210 b.

Benzofurans via 3-chlorocoumarins ←
Perkin transformation
s. *6*, 784

Sodium/alcohol *NaOR*

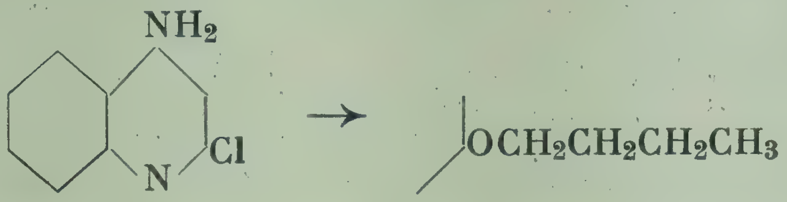
Ethers from halides Hal → OR

245.



2-Bromo-5-ethoxypyridine heated 5 hrs. with a soln. of Na in ethanol at 160° in a sealed tube → 2.5-diethoxypyridine. Y: 90%. F. e. s. H. J. den Hertog, J. P. Wibaut et al., R. *69*, 700, 673 (1950).

246.



2-Chloro-4-aminoquinoline heated with a soln. of Na in abs. n-butanol in a sealed tube at 150° for 24 hrs. → 2-n-butoxy-4-aminoquinoline. Y: 88%. F. e. s. J. Büchi, H. Hurni, and R. Lieberherr, Helv. *32*, 1806 (1949).

Selective replacement of chlorine by alkoxyl Cl → OR

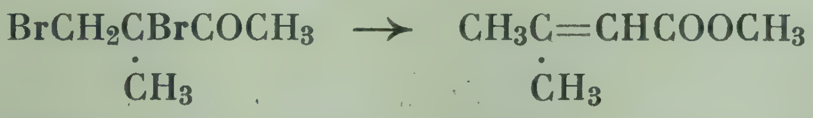
247. $ClCH{=}CHCH_2Cl \rightarrow ClCH{=}CHCH_2OC_2H_5$

trans-1,3-Dichloropropene stirred with a soln. of 1 mole Na in ethanol for 2 hrs. without cooling, whereby the temp. rises to 75° → *trans*-3-ethoxy-1-chloro-1-propene. Y: 76%.—Similarly: *cis*-Isomer. Y: 71%. L. F. Hatch, H. E. Alexander, and J. D. Randolph, J. Org. Chem. *15*, 654 (1950).

Sodium methoxide ←

α,β-Ethylenecarboxylic acid esters ←
from methyl α,β-dibromoketones

248.



$$\underset{CH_3}{BrCH_2CBrCOCH_3} \rightarrow \underset{CH_3}{CH_3C{=}CHCOOCH_3}$$

2 moles of 3,4-dibromo-3-methyl-2-butanone added with stirring and ice-salt cooling at 20° over a 1.5 hr. period to a suspension of 4 moles of Na-methoxide in anhydrous ether, and stirring continued for an additional hr. → methyl β,β-dimethylacrylate. Y: 64%. F. e. s. R. B. Wagner, Am. Soc. *71*, 3214 (1949).

Sodium amide *$NaNH_2$*

s. *5*, 198; s. a. D. Papa, N. Sperber, and M. Sherlock, Am. Soc. *73*, 1279 (1951)

Potassium carbonate K_2CO_3

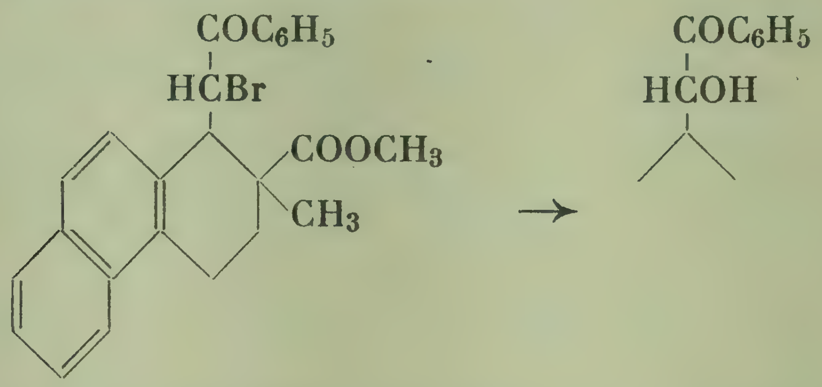
Ethers ROR

s. *2*, 248; *3*, 208; in methyl ethyl ketone s. H. Erdtman and B. Leopold, Acta Chem. Scand. *3*, 1358 (1949); J. H. Barnes et al., Soc. *1950*, 2824

Sodium formate $HCOONa$

Replacement of bromine by hydroxyl Br → OH

249.



cis-1-Benzoylbromomethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene refluxed 24 hrs. with anhydrous Na-formate in anhydrous methanol, the solvent removed, and the residue stirred with water → *cis*-1-benzoylhydroxymethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene. Y: 90%. W. E. Bachmann and F. Ramirez, Am. Soc. *72*, 2525 (1950).

Potassium acetate CH_3COOK

Acetates from halides Hal → OAc

from bromides s. *1*, 211; *3*, 227; from chlorides s. W. Oroshnik and R. A. Mallory, Am. Soc. *72*, 4608 (1950)

Pyridine C_5H_5N

Ethers from halides Hal → OR

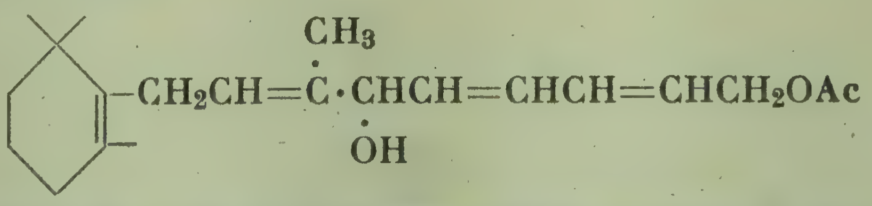
s. *6*, 264

Benzoylation of carbohydrates OH → OAc

s. *6*, 291, 296

Selective acetylation

250.



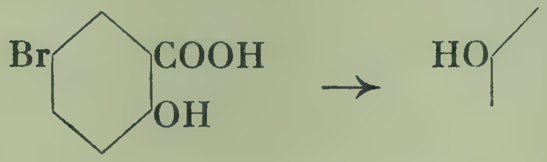
A soln. of acetyl chloride in benzene added during 10 min. with stirring to a soln. of 11.7 gm. 9-(2′,6′,6′-trimethylcyclohex-1′-enyl)-7-methylnona-2,4,7-triene-1,6-diol in dry benzene-pyridine, and stirred for a further 14 hrs. at room temp. → 12.9 gm. 9-acetoxy-1-(2′,6′,6′-trimethylcyclohex-1′-enyl)-3-methylnona-2,5,7-trien-4-ol. I. Heilbron et al., Soc. *1949*, 1516.

Pyridine/silver nitrate s. Silver nitrate/pyridine $C_5H_5N/AgNO_3$

Copper *Cu*

Phenols from halides Hal → OH

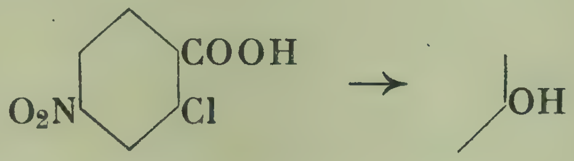
251.



5-Bromosalicylic acid and Cu-powder in 8%-NaOH heated 1.5 hrs. at 140-150° in an autoclave → gentisic acid. Y: 72%. J. Lowenthal and J. M. Pepper, Am. Soc. *72*, 3292 (1950).

Copper/calcium oxide *Cu/CaO*

252.



4-Nitro-2-chlorobenzoic acid, carbonate-free CaO, water, and some Cu-powder heated with shaking at 155-160° under 1000 lbs. N_2 pressure in an autoclave for 6 hrs. → 4-nitrosalicylic acid. Y: 80-86%. E. Wenis and T. S. Gardner, J. Am. Pharm. Assoc. *38*, 9 (1949).

Silver oxide Ag_2O

Glycosides ROR

s. *1*, 217; s. a. N. M. Ferguson and I. H. Gardner, Am. Soc. *72*, 2877 (1950)

Silver carbonate Ag_2CO_3

Methyl glycosides
Königs-Knorr reaction

s. *1*, 218; s. a. H. G. Fletcher, Jr., and C. S. Hudson, Am. Soc. *72*, 4173 (1950)

Steroid glycosides

s. *1*, 219/20; s. a. E. Hardegger and F. G. Robinet, Helv. *33*, 456, 1871 (1950)

Silver acetate CH_3COOAg

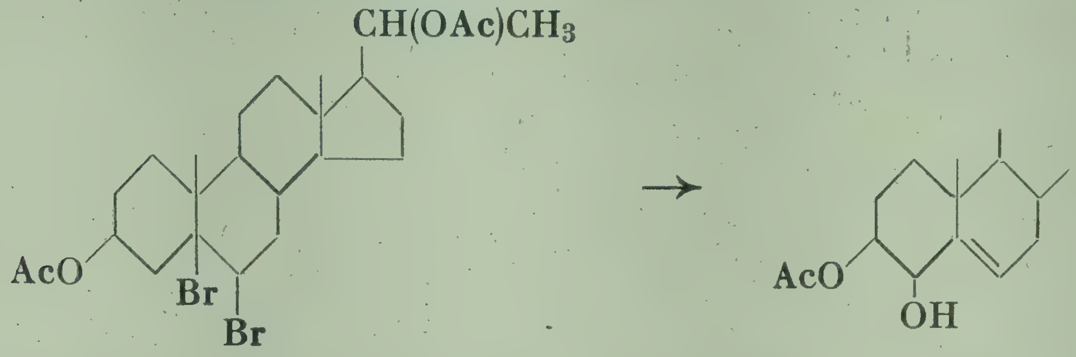
Replacement of bromine by acetoxy groups Br → OAc

s. *1*, 221; *2*, 261; s. a. A. C. Cope and S. W. Fenton, Am. Soc. *73*, 1668 (1951)

Silver nitrate/pyridine *$AgNO_3/C_5H_5N$*

Ethylenealcohols from 1,2-dibromides ←

253.

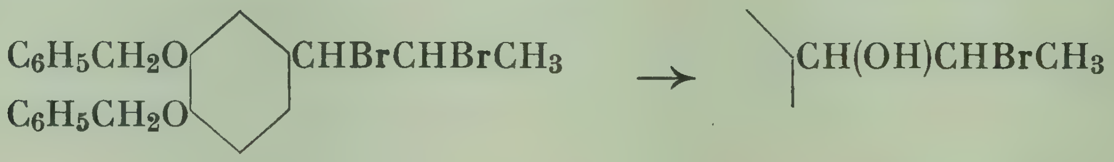


Δ^5-Pregnene-3,20-diol 3,20-diacetate dibromide and $AgNO_3$ in anhydrous pyridine allowed to stand in the dark for 3-5 days with occasional stirring → Δ^5-pregnene-3,4,20-triol 3,20-diacetate. Y: 60%. F. e., with lower yields, s. M. Pesez and A. Petit, Bl. *1949*, 632.

Calcium carbonate *$CaCO_3$*

Bromohydrins from 1,2-dibromides CBrCBr → C(OH)CBr

254.



Precipitated $CaCO_3$ added to a soln. of 1-(3,4-dibenzyloxyphenyl)-1,2-dibromopropane in acetone-water, and heated on a steam bath for 1 hr. → 1-(3,4-dibenzyloxyphenyl)-2-bromo-1-propanol. Y: nearly 100%. J. Kovács and T. Horváth, J. Org. Chem. *14*, 306 (1949).

Hexamethylenetetramine *$C_6H_{12}N_4$*

Aldehydes from halides $CH_2Hal \rightarrow CHO$
Sommelet reaction

255. o-Iodobenzyl bromide and hexamethylenetetramine in chloroform allowed to stand overnight, the salt (Y: 95%) separated, and refluxed in 50%-acetic acid for 2 hrs. → o-iodobenzaldehyde. Y: 76%.—Two substituents in the o-position hinder the reaction, electron-attracting and -repelling groups acting in the same way (Soc. *1949*, 2704). Electron-attracting substituents decrease the rate of the reaction and the yield, even when electron-releasing substituents are also present.—50%-Acetic acid proved to be the best solvent (Soc. *1950*, 2141). F. e. s. S. J. Angyal et al., Soc. *1949*, 2704, 2700; *1950*, 2141; Org. Synth. *30*, 67 (1950); dialdehydes s. J. H. Wood et al., Am. Soc. *72*, 2992 (1950).

Isopropane nitronate ←

s. *5*, 202; s. a. Am. Soc. *71*, 3482 (1949); in acetone-water s. G. Dupont, R. Dulou, and V. Léon, Bl. *1950*, 1313

Stannic chloride *$SnCl_4$*

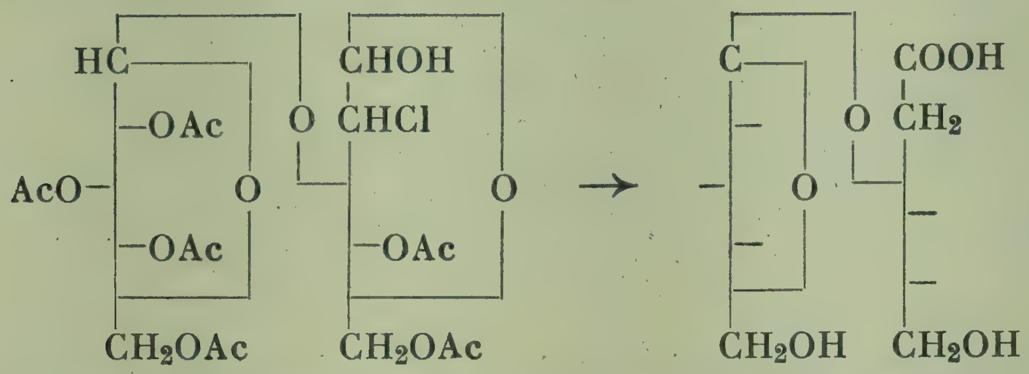
Hydroperoxides from halides Hal → OOH

256. 90%-H_2O_2 added at 0° to ethereal p-nitrotriphenylmethyl chloride, then $SnCl_4$ added dropwise with stirring and ice-cooling, and allowed to stand 2 or more hrs. in an ice bath → p-nitrotriphenylmethyl hydroperoxide (startg. m. f. 319). Y: 61-80%. P. D. Bartlett and J. D. Cotman, Jr., Am. Soc. *72*, 3095 (1950).

Lead oxide *PbO*

Carboxylic acids from halogenhydrins ←

257.



2-Chlorohexaacetylglucosido-3-glucose heated with Pb oxide in water at a gradually rising temp. of 60-100° for 30-35 hrs., and the reaction product isolated as Ca salt → Ca-glucosido-3-glucosaccharinate. Y: 79%. A. M. Gakhokidze, Ж. *19*, 2082 (1949); C. A. *44*, 3914 b.

Sulfur dioxide *SO_2*

Selective O-acylation OH → OAc

s. *4*, 244; s. a. M. *81*, 647 (1950)

Sulfuric acid *H_2SO_4*

Carboxylic acids from 1,1,1-trihalides $CHal_3$ → COOH

258. A mixture of benzotrifluoride and 100%-H_2SO_4 heated cautiously until the benzotrifluoride layer disappears → benzoic acid. Y: 94%. F. e. s. G. M. LeFave, Am. Soc. *71*, 4148 (1949); with $H_2SO_4/ClSO_3H$ s. Am. Soc. *72*, 3308 (1950).

Carboxylic acid esters from 1,1,1-trihalides $CHal_3$ → COOR

259. $C_6H_5CCl_3 \rightarrow C_6H_5COOC_3H_7$

A mixture of benzotrichloride and 100%-H_2SO_4 heated with a smoky flame until the reaction ensues, frequently agitated over a 1 hr. period until the reaction is completed, cooled, poured cautiously with stirring into n-propanol, and gently refluxed for 0.5 hr. → n-propyl benzoate. Y: 81%. F. e. with trifluorides s. G. M. LeFave and P. G. Scheurer, Am. Soc. *72*, 2464 (1950).

Chlorosulfonic acid/sulfuric acid *HSO_3Cl/H_2SO_4*

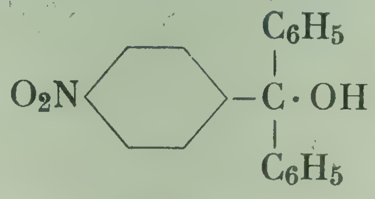
Carboxylic acids from 1,1,1-trihalides $CHal_3$ → COOH

s. *6*, 258

Perchloric acid *$HClO_4$*

Replacement of chlorine by hydroxyl Cl → OH

260.



$HClO_4$ added to a soln. of p-nitrotriphenylmethyl chloride in glacial acetic acid, then poured into a large excess of water → p-nitrotriphenylcarbinol. Y: 78%. P. D. Bartlett and J. D. Cotman, Jr., Am. Soc. *72*, 3095 (1950).

Hydrochloric acid *HCl*

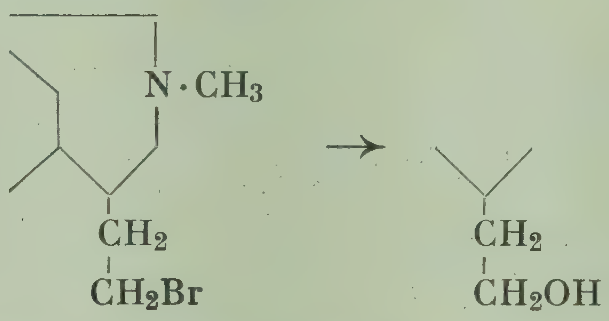
partial replacement

s. *3*, 220; s. a. S. J. Childress and R. L. McKee, Am. Soc. *72*, 4271 (1950)

Hydrobromic acid/sulfuric acid *HBr/H_2SO_4*

Replacement of bromine by hydroxyl Br → OH

261.



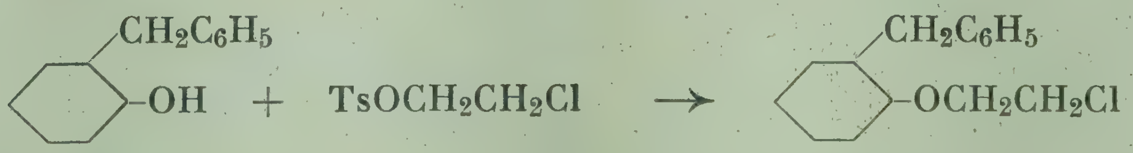
0.5 gm. bromodesoxy-N-methyldihydroisopseudostrychnine hydrobromide (prepn. s. 583) boiled with aq. HBr-H_2SO_4 for 2.5 hrs. → 0.34 gm. N-methyldihydroisopseudostrychnine. F. e. s. H.-G. Boit, B. *83*, 217 (1950).

Sulfur ↑ OC ⇅ S

Sodium hydride *NaH*

Ethers from p-toluenesulfonic acid esters OH → OR

262.



A soln. of o-benzylphenol in toluene added dropwise to a stirred suspension of NaH in toluene under N_2, refluxed 30 min., β-chloroethyl p-toluenesulfonate added dropwise with stirring and refluxing, and worked up after 16 hrs. of refluxing → β-(o-benzylphenoxy)ethyl chloride. Y: 89%. F. e. s. W. B. Wheatley et al., Am. Soc. *72*, 1655 (1950).

Alkali hydroxide ←

Replacement of sulfonic acid groups by hydroxyl $SO_3H \rightarrow OH$

s. *3,* 229; s. a. M. F. Clarke and L. N. Owen, Soc. *1950,* 2108

Sodium hydroxide *NaOH*

Hydroxy compounds from sulfones $SO_2R \rightarrow OH$

s. *6,* 484

Sodium hydroxide/potassium hydroxide *NaOH/KOH*

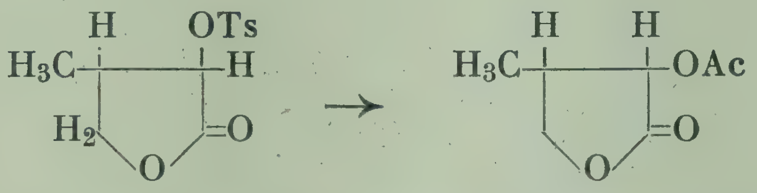
Replacement of sulfonic acid groups by hydroxyl $SO_3H \rightarrow OH$

s. *2,* 268; s. a. R. N. Shreve and F. R. Lloyd, Ind. Eng. Chem. *42,* 811 (1950)

Sodium acetate *CH_3COONa*

Acetates from tosylates ←
Epimerization

263.

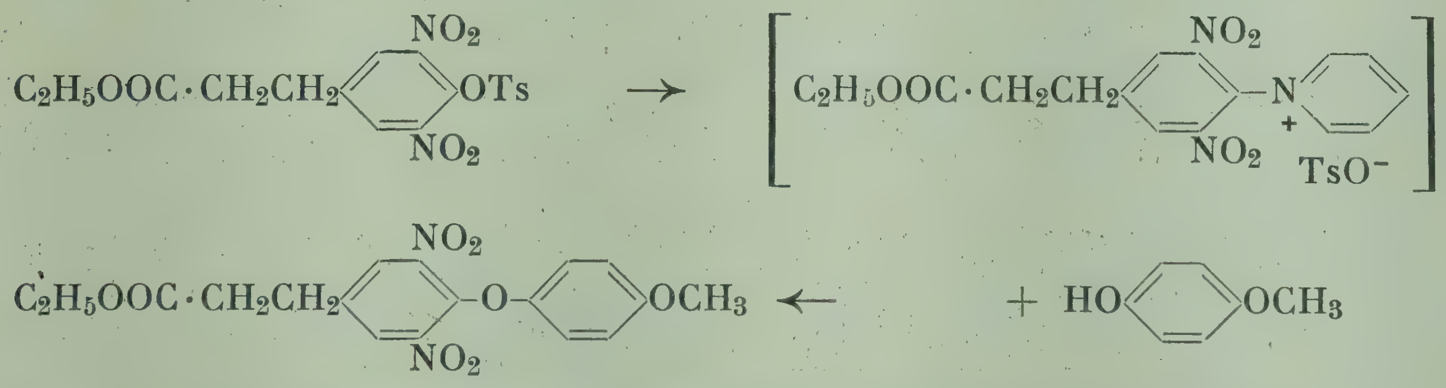


A mixture of *trans*-α-tosyloxy-β-methyl-γ-lactone, freshly fused Na-acetate, glacial acetic acid, and acetic anhydride refluxed 7 hrs. → *cis*-α-acetoxy-β-methyl-γ-lactone. Y: 70%. F. Fleck and H. Schinz, Helv. *33,* 140 (1950).

Pyridine *C_5H_5N*

Ethers from tosylates and halides via quaternary pyridinium salts ←

264.



Ethyl β-(3,5-dinitro-4-p-tolylsulfonyloxyphenyl)propionate and quinol monomethyl ether refluxed in pyridine for 1 hr. → ethyl β-(3,5-dinitro-4-p-methoxyphenoxyphenyl)propionate. Y: 95%.—Similarly, other quaternary salts, e.g. from halides, yield the ethers. F. e. s. E. T. Borrows et al., Soc. *1949,* S190, S199.

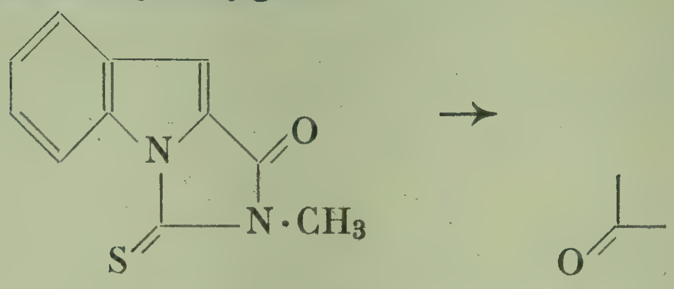
Phosphorus/hydroiodic acid s. Hydroiodic acid/phosphorus *P/HI*

Hydrogen peroxide *H_2O_2*

Replacement of sulfur by oxygen

C:S → C:O

265.



A hot alc. soln. of 0.3 gm. 2-thio-3-methylindolo(1′,2′,1,5)hydantoin treated with 30%-H_2O_2, then with methanolic KOH → 0.25 gm. 3-methylindolo(1′,2′,1,5)hydantoin. J. A. Elvidge and F. S. Spring, Soc. *1949,* S135; C^{14}-compounds s. C. Heidelberger and R. B. Hurlbert, Am. Soc. *72,* 4704 (1950).

Sulfuric acid *H_2SO_4*

Carbohydrate acetates from carbohydrate sulfuric acid esters

←

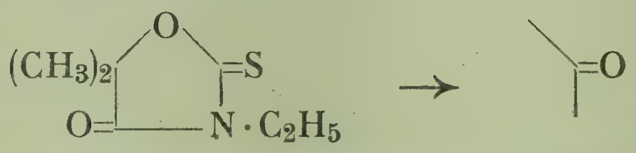
266. Acetic anhydride added during 5–8 hrs. below –10° in a CO_2-atmosphere to a mixture of 0.85 g. Na D-glucose 6-sulfate and abs. H_2SO_4, then kept tightly stoppered at –15 to –20° for 14–16 hrs., and ca. 4 hrs. at room temp. → 0.90 g. α-D-glucopyranose pentaacetate.—The reaction takes place without Walden inversion but with some glycosidic hydrolysis. F. e. s. M. L. Wolfrom and R. Montgomery, Am. Soc. *72,* 2859 (1950).

Chlorine *Cl*

Replacement of sulfur by oxygen

C:S → C:O

267.



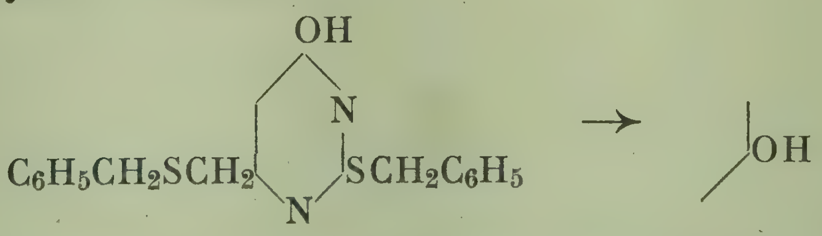
2-Thio-5,5-dimethyl-3-ethyloxazolid-4-one in CCl_4 stirred with water, Cl_2 passed through for ¾ hr. below 10°, and excess Cl_2 removed by a current of air → 5,5-dimethyl-3-ethyloxazolid-2,4-dione. Y: 90%. F. e. s. J. S. H. Davies, W. H. Hook, and F. Long, Soc. *1950,* 36.

Hydrochloric acid *HCl*

Partial hydrolysis of thioethers

←

268.

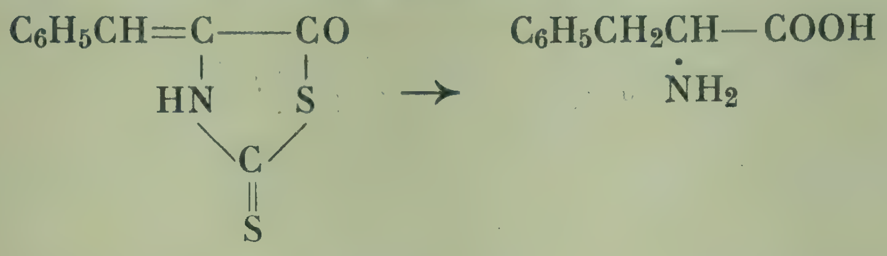


A soln. of 2-benzylthio-4-benzylthiomethyl-6-hydroxypyrimidine in HCl-acetic acid-water heated 2.5 hrs. on a steam bath → 2,6-dihydroxy-4-benzylthiomethylpyrimidine. Y: 98.7%. F. e. s. R. M. Dodson, E. R. Peterson, and J. K. Seyler, Am. Soc. *72,* 3281 (1950).

Hydroiodic acid/phosphorus *HI/P*

α-Aminocarboxylic acids from thiazolidones ↻

269.



Red P, followed by 40%-aq.-HI added to a suspension of 2-thio-4-benzylidenethiazolid-5-one in glacial acetic acid, and refluxed 1.5 hrs. → β-phenylalanine. Y: 70%. F. e. s. J. D. Billimoria and A. H. Cook, Soc. *1949*, 2323.

Remaining Elements ↑ OC ⇵ Rem

Sodium salt *Na+*

Carboxylic acid esters from carboxylic acids COOH → COOR
Labeled compounds

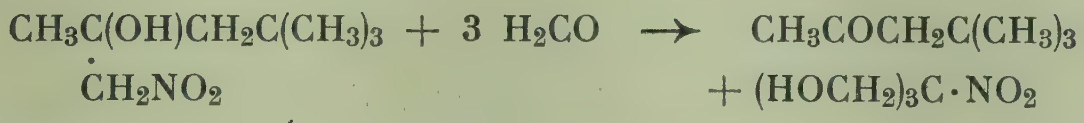
270. A mixture of Na-acetate-2-C^{14} and n-butyl phosphate refluxed 1 hr. at 140-220° → n-butyl acetate-2-C^{14}. Y: 82%.—Alkyl phosphates have been found to be somewhat superior to the use of the corresponding alkyl sulfates which boil slightly lower and are much less stable at temp. near 200°. F. e. s. G. A. Ropp, Am. Soc. *72*, 2299 (1950).

Carbon ↑ OC ⇵ C

Sodium hydroxide *NaOH*

Ketones from nitroalcohols ←

271.



$$\underset{CH_2NO_2}{CH_3C(OH)CH_2C(CH_3)_3} + 3\ H_2CO \rightarrow CH_3COCH_2C(CH_3)_3 + (HOCH_2)_3C\cdot NO_2$$

1-nitro-2,4,4-trimethylpentan-2-ol treated with paraformaldehyde in alcohol with the addition of a small pellet of NaOH, and the volatile material distilled off at 25° in vacuo → nitrotri(hydroxymethyl)-methane (Y: 92.7%) and 4,4-dimethylpentan-2-one (Y: 73.2%). H. Baldock, N. Levy, and C. W. Scaife, Soc. *1949*, 2627.

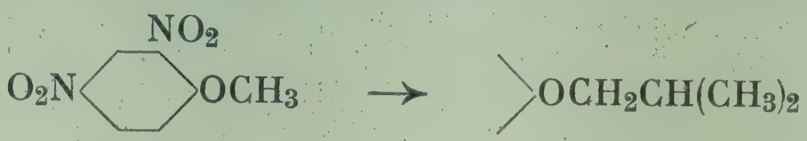
Carboxylic acids from α-halogenoketones via pyridinium salts $COCH_2Br \rightarrow COOH$
Degradation with loss of 1 C-atom

s. *1*, 789; *2*, 833; s. a. R. B. Wagner and J. M. Tome, Am. Soc. *72*, 3477 (1950); R. T. Arnold, K. Murai, and R. M. Dodson, Am. Soc. *72*, 4193 (1950)

Potassium hydroxide *KOH*

Transetherification of activated ethers OR → OR′

272.

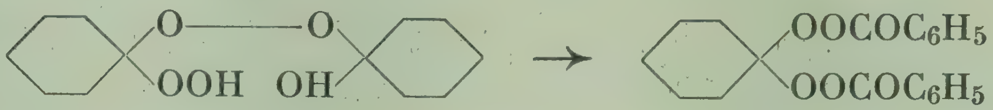


2,4-Dinitroanisole added to a soln. of KOH in isobutyl alcohol, and refluxed 10 hrs. → 2,4-dinitrophenyl isobutyl ether. Y: 77%. F. e. s. Y. Ogata and M. Okano, Am. Soc. *71*, 3211 (1949).

Pyridine *C_5H_5N*

1,1-Di(acylperoxy) compounds from hydroxy hydroperoxy peroxides ←

273.



1-Hydroxy-1′-hydroperoxydicyclohexyl peroxide added with ice-cooling to a mixture of benzoyl chloride and abs. pyridine, then allowed to stand overnight → 1,1-di(benzoperoxy)cyclohexane. Y: 91%. R. Criegee, W. Schnorrenberg, and J. Becke, A. *565*, 7 (1949).

Zinc/ozone s. Ozone/zinc *Zn/O_3*

Mercuric acetate *$(CH_3COO)_2Hg$*

Carboxylic acid esters from carboxylic acids COOH → COOR
Transacylation

274. Caprylic acid, vinyl acetate, a trace of Cu-resinate, and mercuric acetate added in that order, then stirred vigorously, a little H_2SO_4 added, stirring continued until a homogeneous soln. results, allowed to stand at 30° for 72 hrs., Na-acetate added with good stirring, and distilled → vinyl caprylate. Y: 95% based on recoverable material. Conversion: 72.5%.—By keeping the temp. low (20-30°) the formation of ethylidene diesters is avoided. F. e. s. R. L. Adelman, J. Org. Chem. *14*, 1057 (1949); s. a. D. Swern and E. F. Jordan, Org. Synth. *30*, 106 (1950).

Peracetic acid/p-toluenesulfonic acid s.
p-Toluenesulfonic acid/peracetic acid *$CH_3COO_2H/TsOH$*

Lead tetraacetate *$(CH_3COO)_4Pb$*

Oxidative cleavage ←
Oxo compounds from glycols

275.

$$CH_3[CH_2]_7CH{=}CH[CH_2]_7CH(OH)CH(OH)[CH_2]_7CH{=}CH[CH_2]_7CH_3$$
$$\rightarrow\ 2\ CH_3[CH_2]_7CH{=}CH[CH_2]_7CHO$$

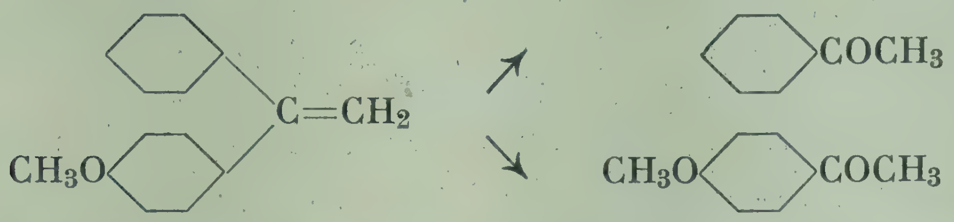
Hexatriaconta-9,27-diene-18,19-diol and the theoretical quantity of Pb-tetraacetate in abs. benzene under dry N_2 shaken at room temp. for

0.5 hr. → olealdehyde. Y: above 90%. F. e. s. F. Bouquet and C. Paquot, Bl. *1949*, 440; ketones s. J. D. Roberts and C. W. Sauer, Am. Soc. *71*, 3925 (1949).

Sodium azide *NaN_3*

Ketones from 1,1-diarylethylenes ←
Schmidt reaction
Migration aptitude

276.



Concd. H_2SO_4 added dropwise with stirring and ice-cooling to a suspension of NaN_3 in chloroform, then a soln. of 1-p-anisyl-1-phenylethylene in chloroform added at 25° dropwise, with stirring, in the course of several hrs., stirring continued for another hr., and allowed to stand overnight → acetophenone (Y: 49%) and p-methoxyacetophenone (Y: 8%).—The reaction involves a migration of an aryl group from a carbon to a nitrogen atom. The order of migratory aptitude follows the sequence p-anisyl > p-tolyl > p-biphenyl > phenyl > p-chlorophenyl > methyl, and is in qualitative agreement with the sequence found in the pinacol-pinacolone rearrangement of sym. pinacols. F. e. s. W. E. McEwen, M. Gilliland, and B. I. Sparr, Am. Soc. *72*, 3212 (1950); s. a. L. P. Kuhn and J. D. Domenico, Am. Soc. *72*, 5777 (1950).

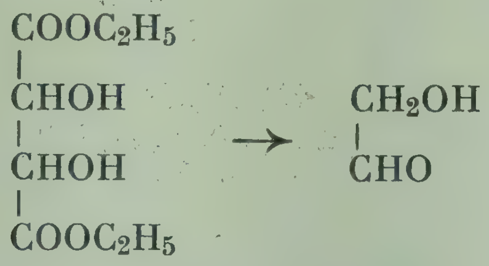
p-Toluenesulfonic acid *TsOH*

Transesterification COOR → COOR′
s. *4*, 263; s. a. W. S. Emerson and R. A. Heimsch, Am. Soc. *73*, 1297 (1951)

Sodium bismuthate *$NaBiO_3$*

Oxidative cleavage and degradation ←
Oxo compounds from glycols, acyloins, and α-hydroxycarboxylic acids

277.



$$\begin{array}{l} COOC_2H_5 \\ | \\ CHOH \\ | \\ CHOH \\ | \\ COOC_2H_5 \end{array} \rightarrow \begin{array}{l} CH_2OH \\ | \\ CHO \end{array}$$

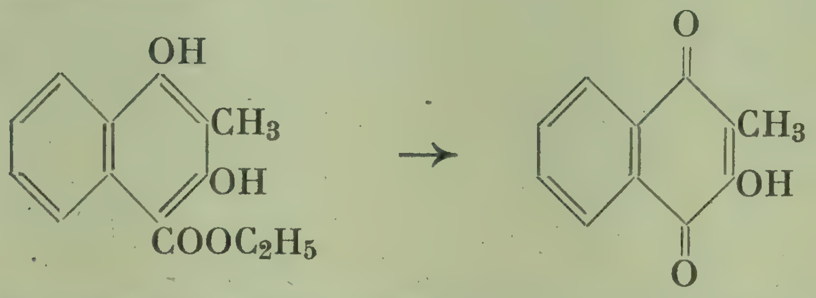
Na-bismuthate in an acid medium smoothly and selectively effects oxidations similar to those brought about by Pb-tetraacetate and HIO_4; 1,2-glycols undergo fission to aldehydes or ketones, acyloins to the derived carbonyl compounds and carboxylic acids, and α-hydroxycarboxylic acids to the lower aldehyde or ketone, all in good yield.

Aldehydes are not further oxidized.—E: Ethyl tartrate and Na-bismuthate in aq. H_3PO_4 shaken 3.5 hrs. at 17-18° → glycolaldehyde (isolated as phenylhydrazone). Y: 94%. F. e. s. W. Rigby, Soc. *1950*, 1907.

Oxygen O_2

Hydroxynaphthoquinones ←

278.

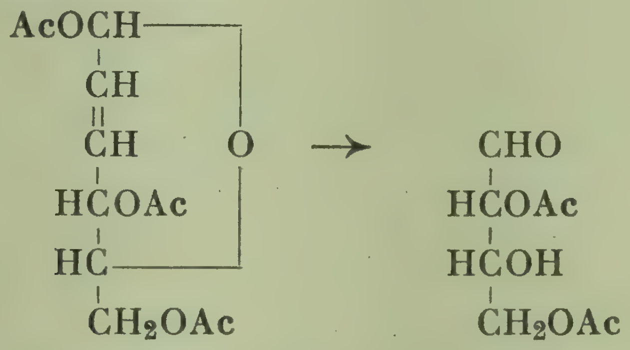


Ethyl 1,3-dihydroxy-2-methylnaphthalene-4-carboxylate and 6%-NaOH shaken with O_2 for 2 hrs. → phthiocol (3-hydroxy-2-methylnaphthoquinone). Y: 75%. O. Neunhoeffer and H. v. Hörner, Chem. B. *83*, 99 (1950).

Ozone O_3

Aldehydes from ethylene derivatives ←
Degradation of carbohydrates

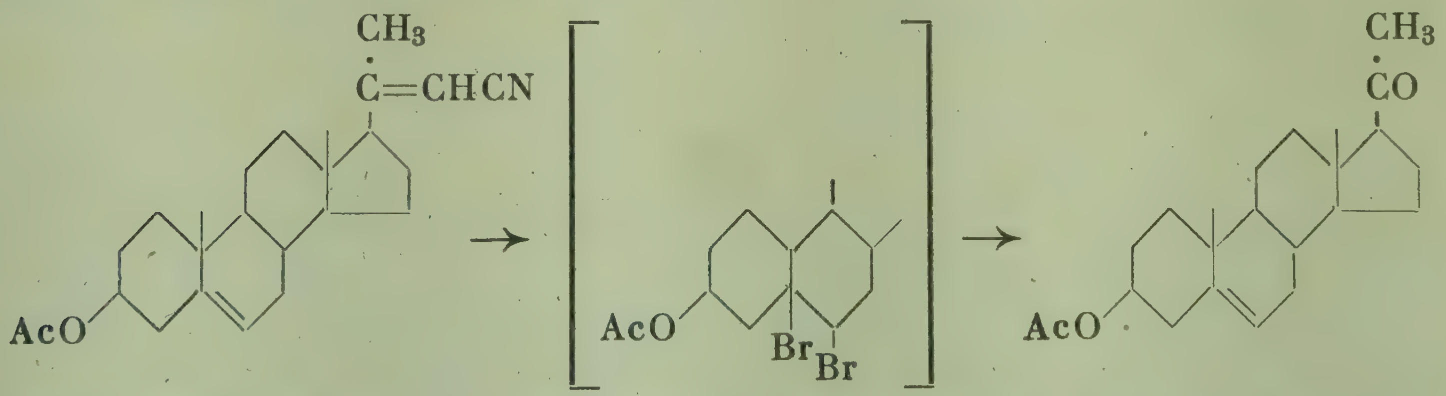
279.



A stream of O_2-O_3 passed through a soln. of 1,4,6-triacetyl pseudoglucal at 12° until it no longer decolorized a soln. of Br_2 in CCl_4, after dilution with ether, Zn-dust added, and the mixture refluxed until the soln. failed to color starch-iodide paper → 2,4-diacetyl-D-erythrose. Y: 95.4%. W. G. Overend, M. Stacey, and L. F. Wiggins, Soc. *1949*, 1358.

Ketones from ethylene derivatives
with protection of a double bond

280.

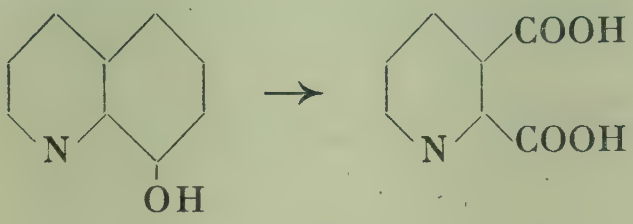


A soln. of Br_2 in chloroform added dropwise with stirring to an ice-cooled soln. of 0.5 gm. 22-cyanobisnor-5,20;22-choladiene-3β-ol acetate

(m. p. 182°), a stream of O_3-O_2 passed through for 26 min., the solvent removed in vacuo, the residue taken up in glacial acetic acid-ether, then shaken and refluxed with Zn dust for 10 min. → 0.46 gm. crude 5-pregnene-3β-ol-20-one acetate. M. E. Herr and F. W. Heyl, Am. Soc. *72*, 1753 (1950); protection of a double bond s. a. P. Wieland and K. Miescher, Helv. *32*, 1922 (1949).

Oxydative ring opening C

281.



A soln. of 8-hydroxyquinoline in glacial acetic acid subjected to a stream of 9-10% ozonized oxygen at 20 l. per hr., for 48 hrs. at room temp., then 30%-H_2O_2 added cautiously, and refluxed 2 hrs. → quinolinic acid. Y: 92%. F. e. with lower yields s. A. F. Lindenstruth and C. A. VanderWerf, Am. Soc. *71*, 3020 (1949).

Ozone/zinc *O_3/Zn*

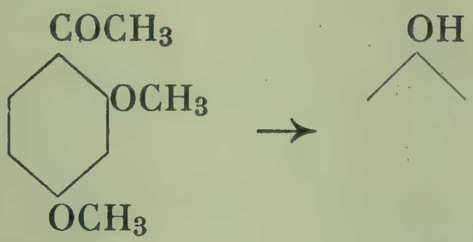
Aldehydes from ethylene derivatives ←
Degradation of carbohydrates with loss of 1 C-atom

282. Oxygen containing 3-5% ozone introduced into a soln. of hexaacetylglucosido-3-glucal (prepn. s. 887) in glacial acetic acid, after completion of the reaction diluted with ether, Zn dust added, and heated on a water bath with shaking → hexaacetyl-α-glucosido-2-arabinose. Y: 69%. A. M. Gakhokidze, Ж. *19*, 2082 (1949); C. A. *44*, 3914b.

p-Toluenesulfonic acid/peracetic acid *TsOH/CH_3COO_2H*

Hydroxy compounds from ketones COR → OH
Oxidative degradation

283.

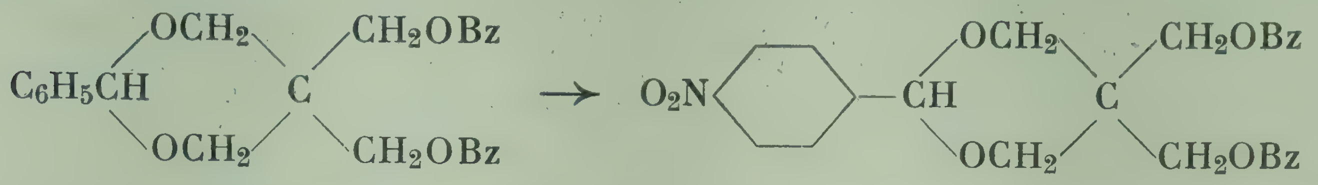


A soln. of 2,4-dimethoxyacetophenone, 20-22%-peracetic acid, and a trace of p-toluenesulfonic acid in glacial acetic acid warmed 0.5 hr. at 35°, then 3 hrs. at 60—65°, more peracetic acid added, and allowed to stand 24 hrs. → 1-hydroxy-2,4-dimethoxybenzene. Y: 54%. A. Ballio, G. *79*, 924 (1949); cf. W. v. E. Doering and L. Speers, Am. Soc. *72*, 5515 (1950).

α-Naphthalenesulfonic acid ←

Transacetalization ←

284.

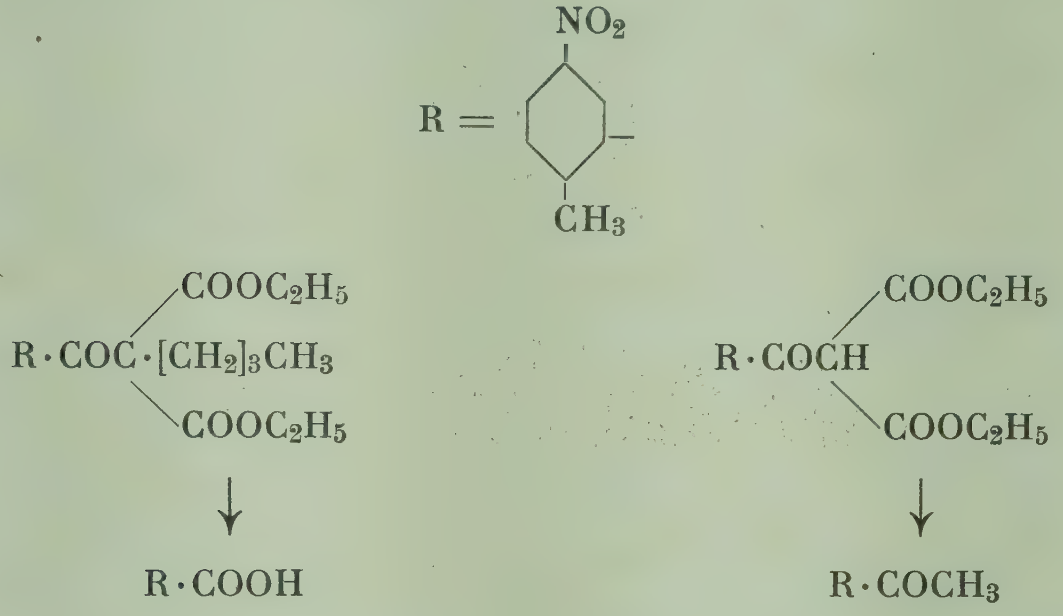


A mixture of benzalpentaerythritol dibenzoate, p-nitrobenzaldehyde, α-naphthalenesulfonic acid, and benzene refluxed for 6 hrs. → (p-nitrobenzal)pentaerythritol dibenzoate. Y: 93%. F. e. s. E. Bograchov, Am. Soc. *72,* 2268 (1950).

Sulfuric acid *H_2SO_4*

Carboxylic acids and methyl ketones from acylmalonic acid esters ←

285.



Diethyl 2-methyl-5-nitrobenzoyl-n-butylmalonate	Diethyl 2-methyl-5-nitrobenzoylmalonate

heated with a 2:1:6 mixture of concd. H_2SO_4-water-acetic acid in an oil bath at 105–110° for 3 hrs.

2-methyl-5-nitrobenzoic acid. Y: 91%.	2-methyl-5-nitroacetophenone. Y: 95%.

M. E. Blumer and E. Sorkin, Helv. *32,* 2547 (1949).

Hypohalites *$HalO^-$*

Carboxylic acids from ketones COR → COOH
Oxidative degradation

286. If alkaline hypobromite soln. is to be used successfully for the oxidation of the higher alkyl aryl ketones to acids, the ketone should have 2 H-atoms on the C-atom adjacent to the carbonyl group. E. s. R. Levine and J. R. Stephens, Am. Soc. *72,* 1642 (1950).

Hypochlorites *ClO^-*

Haloform reaction
Carboxylic acids from methyl ketones $COCH_3 \rightarrow COOH$
Degradation with loss of 1 C-atom

s. *1*, 237; large batches s. D. T. Mowry and E. L. Ringwald, Am. Soc. *72*, 2037 (1950)

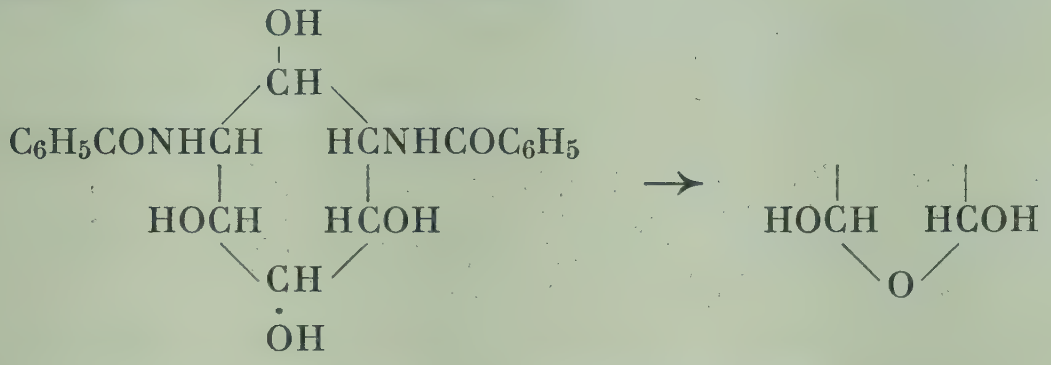
Periodate *IO_4^-*

Oxidative cleavage of the carbon chain ←

s. *3*, 238; s. a. C. F. Huebner and K. P. Link, Am. Soc. *72*, 4812 (1950)

Pyran ring from cyclohexane ring ←

87.

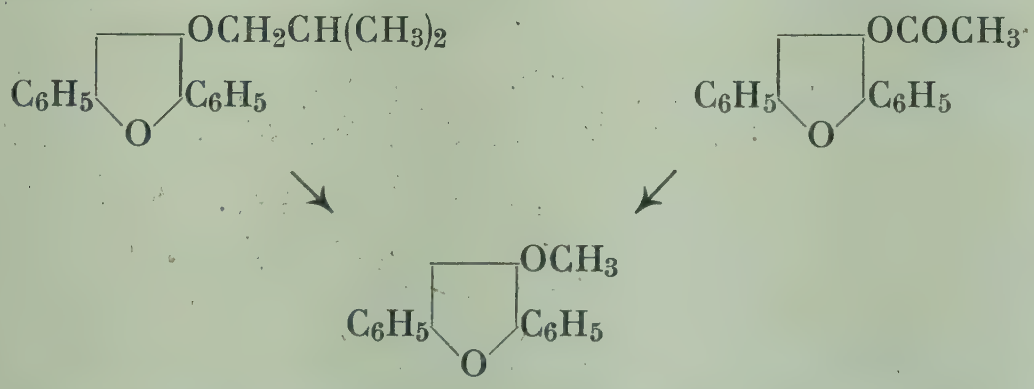


N,N′-Dibenzoylstreptamine and Na-metaperiodate ($NaIO_4$) in 50%-methanol allowed to stand at room temp. for 12-15 hrs. until ca. 2 moles of periodate per mole of sample have been consumed, then the excess periodate and the iodate formed removed by precipitation with Pb-nitrate → 2,4,6-trihydroxy-3,5-dibenzamidotetrahydropyran. Y: 83.5%. H. E. Carter, Y. H. Loo, and J. W. Rothrock, J. Biol. Chem. *179*, 1027 (1949).

Triethylamine hydrochloride *$(CH_3)_3N,HCl$*

Transetherification ←
Ethers from carboxylic acid esters
3-Alkoxyfurans

88.



3-Isobutoxy-2,5-diphenylfuran | 3-Acetoxy-2,5-diphenylfuran

refluxed 30 hrs. with methanol containing HCl
and triethylamine hydrochloride at a pH of 2-3 →
3-methoxy-2,5-diphenyl-furan

Y: 76% with 20% recovery of starting material. | Y: 96%

F. e. s. P. S. Bailey and J. D. Christian, Am. Soc. *71*, 4122 (1949).

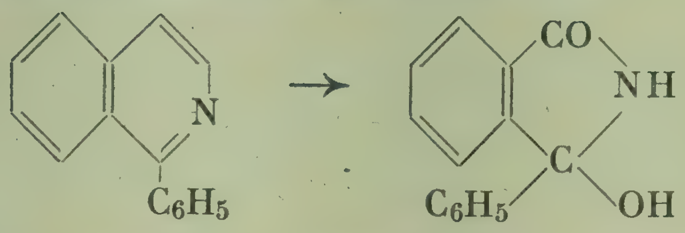
Potassium permanganate *$KMnO_4$*

Aldonic acids from glycals ←

s. *6*, 322

3-Hydroxyphthalimidines from isoquinolines ←

289.



Aq. $KMnO_4$ gradually added during 2 hrs. to a stirred refluxing suspension of 1 gm. 1-phenylisoquinoline in water → 0.7 gm. 3-hydroxy-3-phenylphthalimidine. W. Davies, T. H. Ramsay, and E. R. Stove, Soc. *1949*, 2633.

Potassium permanganate/pyridine *$KMnO_4/C_5H_5N$*

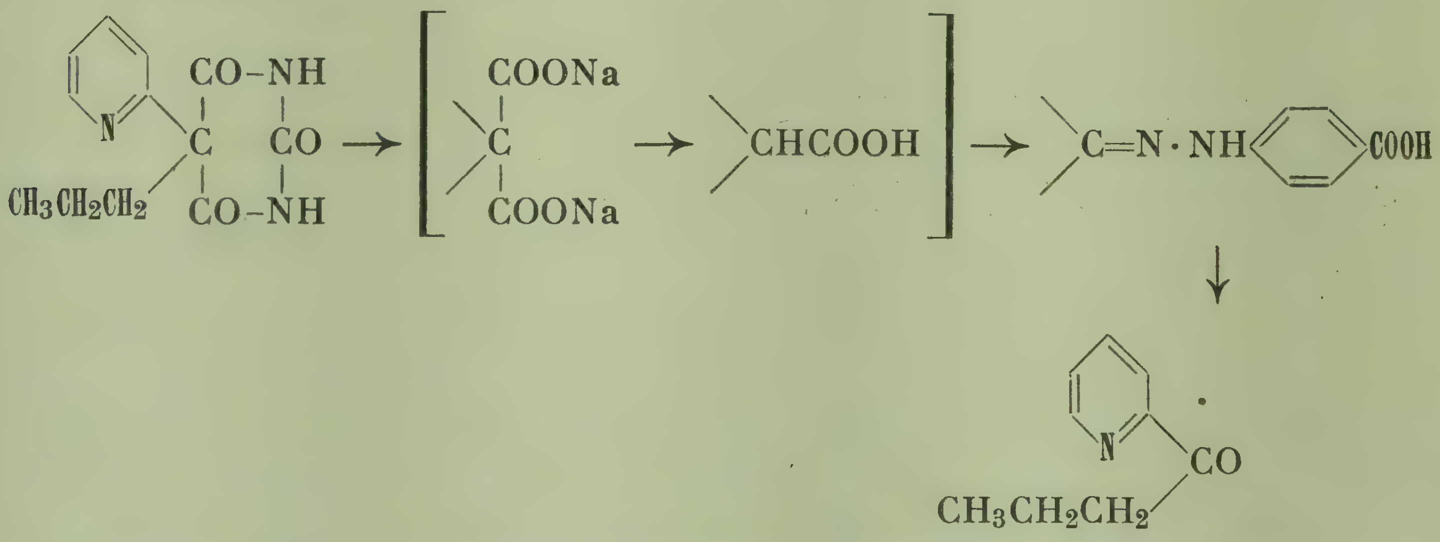
Carboxylic acids from ethylene derivatives $CH{:}C \rightarrow COOH$

s. *6*, 135

Via intermediates *v.i.*

Ketones from barbituric acids
via carboxylic acids and hydrazones
Japp-Klingemann reaction ←

290.



5-n-Propyl-5-(2′-pyridyl)barbituric acid heated in 20% aq. NaOH on a steam cone for 1 hr., evaporated to dryness, redissolved in water, acidified with concd. HCl just before the addition of a p-carboxybenzenediazonium chloride soln. from p-aminobenzoic acid, followed by aq. Na-acetate below 5°, and allowed to stand 96 hrs. at 4° → 2-n-butyrylpyridine p-carboxyphenylhydrazone (Y: 94%) refluxed 1 hr. with pyruvic acid in aq. acetic acid → 2-n-butyrylpyridine (Y: 81%).—F. e. for the Japp-Klingemann reaction s. R. L. Frank and R. R. Phillips, Am. Soc. *71*, 2804 (1949).

Carboxylic acids from hydrocarbons $CH_3 \rightarrow COOH$

s. *6*, 135

Transacylation of glycosides $OAc \rightarrow OAc'$

291. A soln. of methyl β-D-mannopyranoside tetraacetate in anhydrous methanol treated with 2 *N* Ba-methoxide, after 21 hrs. at room temp. concentrated in vacuo at 35° to a syrup which is then dissolved in dry pyridine, cooled in an ice bath, slowly treated with benzoyl chloride, and held at 60° for 2.5 hrs. → methyl β-D-mannopyranoside tetrabenzoate. Y: 81%. R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, Am. Soc. *72*, 2200 (1950); deacylation s. a. *72*, 4173.

Elimination

Hydrogen ↑ OC ⇑ H

Copper *Cu*

Carboxylic acids from alcohols via aldehydes $CH_2OH \rightarrow CHO \rightarrow COOH$

292. Methallyl alcohol and O_2 passed at 300-350° over a copper gauze catalyst → methacrolein (Y: 95.3% based on alcohol consumed; conversion 71%) kept ca. 5 hrs. in a rocking bomb under a pressure of 210 lbs. of oxygen in the presence of a mixture of Cu- and Ni-acetates → methacrylic acid (startg. m. f. 213) (Y: over 96%; conversion ca. 61%). J. M. Church and L. Lynn, Ind. Eng. Chem. *42*, 768 (1950).

Cupric acetate $(CH_3COO)_2Cu$

Oxidation of acyloins $CH(OH)CO \rightarrow COCO$

s. *2*, 287; s. a. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, Soc. *1950*, 2743

Aluminum alkoxide $Al(OR)_3$

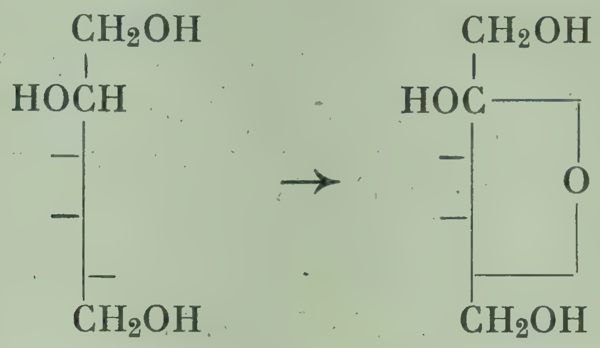
Oxo compounds from alcohols
Oppenauer oxidation $CHOH \rightarrow CO$

s. *1*, 157/8; *2*, 286; stability of β-aminoalcohols toward the oxidation s. R. E. Lutz and R. L. Wayland, Jr., Am. Soc. *73*, 1639 (1951)

Acetobacter suboxydans ←

Carbohydrates from polyalcohols ←
Biochemical oxidation

293.



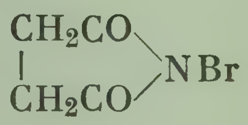
Talitol, Difco yeast extract, and some glycerol in water kept 6 days at 30° in the presence of a culture of Acetobacter suboxydans, and worked up using Pb-acetate to remove the proteins and IR-100 ion exchange resin to remove the Pb-ions → D-tagatose. Y: 75–84%. E. L. Totton and H. A. Lardy, Am. Soc. *71,* 3076 (1949).

N-Bromoacetamide *$CH_3CONHBr$*

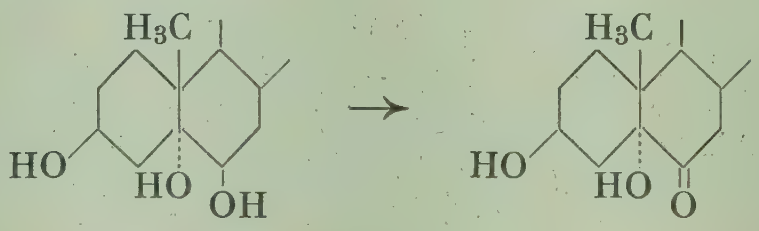
Ketones from sec. alcohols CHOH → CO

s. *4,* 269; s. a. B. A. Koechlin, T. H. Kritchevsky, and T. F. Gallagher, J. Biol. Chem. *184,* 393 (1950)

N-Bromosuccinimide



294.



Selective oxidation. Cholestane-3β,5α,6β-triol, N-bromosuccinimide, ether, methanol, and water shaken a few min. until dissolved → cholestane-3β,5α-diol-6-one. Y: 96,5%. F. e. s. L. F. Fieser and S. Rajagopalan, Am. Soc. *71,* 3938, 3935 (1949).

Lead tetraacetate *$(CH_3COO)_4Pb$*

Benzoxazoles from azomethines ○

s. *6,* 503

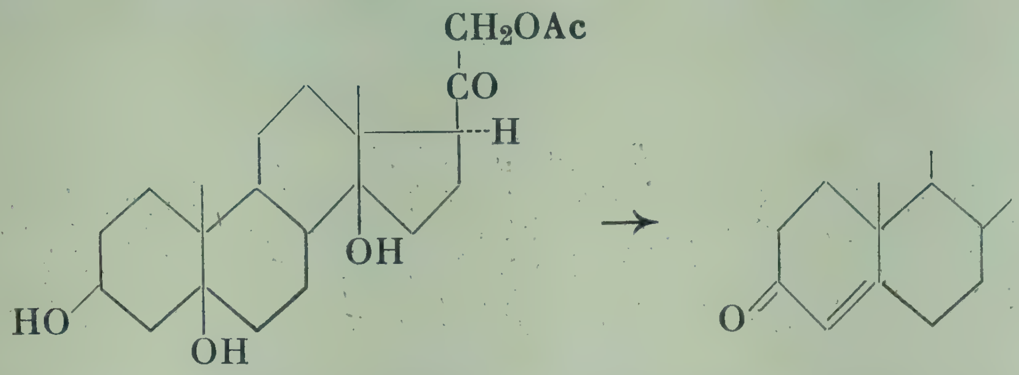
Chromic acid *CrO_3*

Ketones from sec. alcohols CHOH → CO

s. *1,* 167; *4,* 129; s. a. W. A. Mosher und E. O. Langerak, Am. Soc. *73,* 1302 (1951)

α,β-Ethyleneketones from 1,3-diols ←

95.



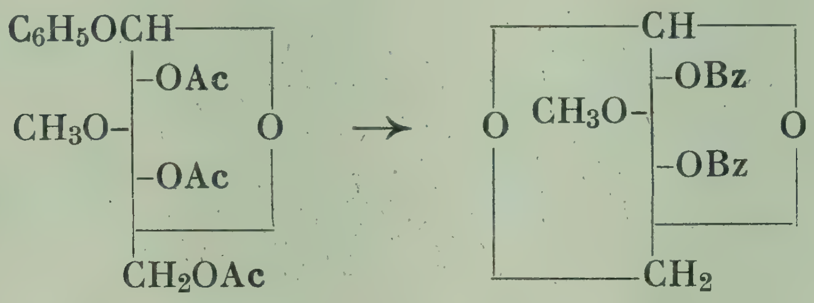
505 mg. 21-acetoxy-3β,5,14-trihydroxy-14-isopregnan-20-one and CrO_3 in glacial acetic acid allowed to stand at 18° for 16 hrs. → 370 mg. 14-hydroxy-14-iso-11-desoxycorticosterone acetate. F. e. s. A. Lardon, Helv. *32*, 1517 (1949).

Oxygen ↑ **OC ⇑ O**

Sodium hydroxide *NaOH*

Anhydrosugars from glycosides ○

296.



Phenyl 3-methyltriacetyl-β-D-glucoside in 2.6 *N* ethanolic NaOH refluxed for 40 hrs., neutralized, the solvent evaporated, the residue and benzoyl chloride in anhydrous pyridine kept at 60° for 2 hrs., then at room temp. overnight → 3-methyl-2,4-dibenzoyllevoglucosan. Y: 82%. M. P. Bardolph and G. H. Coleman, J. Org. Chem. *15*, 169 (1950).

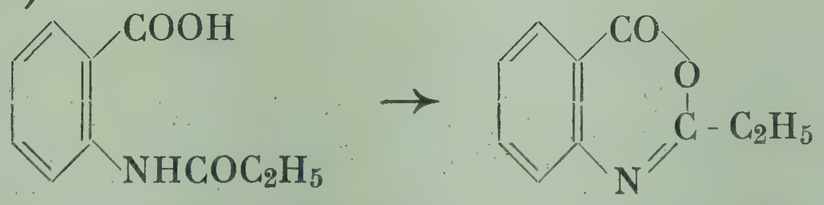
Acetic anhydride *$(CH_3CO)_2O$*

Dicarboxylic acid anhydrides from dicarboxylic acids

297. A mixture of dry homophthalic acid (prepn., s. 188) and acetic anhydride refluxed for 2 hrs. → homophthalic anhydride. Y: 85-88%. O. Grummitt, R. Egan, and A. Buck, Org. Synth. *29*, 49 (1949); s. a. E. C. Horning and A. F. Finelli, Org. Synth. *30*, 81 (1950); J. C. Roberts and B. Shaw, Soc. *1950*, 2842.

3,1,4-Benzoxazones (Acylanthranils)

298.



0.05 mole of N-propionylanthranilic acid and 90-100%-acetic anhydride refluxed 1 hr., then slowly distilled below 139° until ca. 25 ml. is collected, and the remaining acetic anhydride removed under reduced pressure → 2-ethyl-3,1,4-benzoxazone (startg. m. f. 406). Y: 74.7%. F. e. s. D. T. Zentmyer and E. C. Wagner, J. Org. Chem. *14*, 967 (1949).

Acetyl chloride *CH_3COCl*

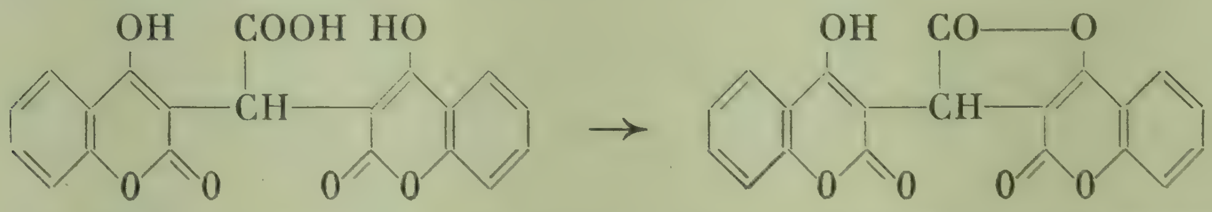
Dicarboxylic acid anhydrides from dicarboxylic acids

299. α,α′-Diphenylsuccinic acid refluxed with glacial acetic acid and acetyl chloride until all of the acid is dissolved, then distilled in vacuo → α,α′-diphenylsuccinic acid anhydride. Y: 80-87%. J. A. McRae, R. A. B. Bannard, and R. B. Ross, Can. J. Research *28B*, 73 (1950); s. a. J. Cason, G. Sumvell, and R. S. Mitchell, J. Org. Chem. *15*, 850 (1950).

Thionyl chloride *$SOCl_2$*

Lactones from hydroxycarboxylic acids

300.

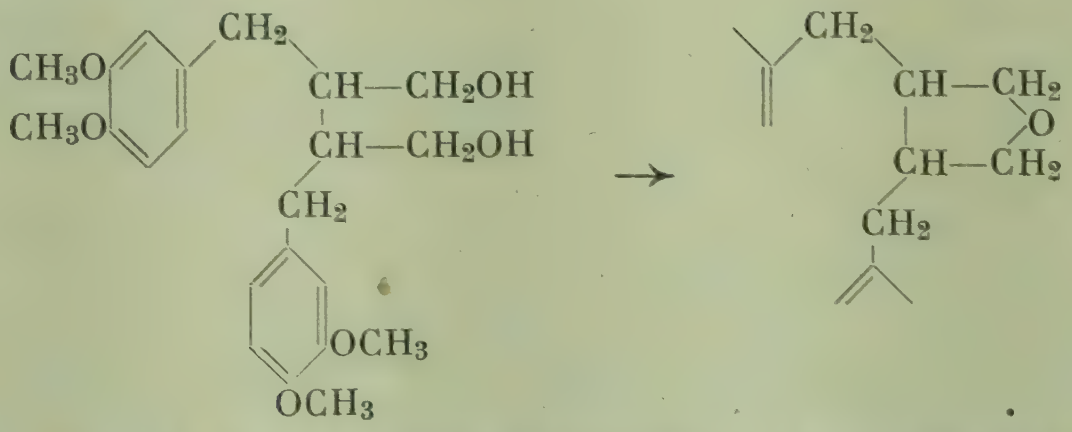


1 gm. di-(4-hydroxycoumarinyl-3)-acetic acid boiled with $SOCl_2$ for several min. → 0.93 gm. lactone. K. Fučik et al., Bl. *1949*, 609.

Potassium hydrogen sulfate *$KHSO_4$*

Tetrahydrofurans

301.



0.06 gm. *meso*-1,4-di-(3,4-dimethoxyphenyl)-2,3-di(hydroxymethyl)-butane heated 0.5 hr. with $KHSO_4$ at 180° → 0.05 gm. *meso*-3,4-di-(3,4-dimethoxybenzyl)tetrahydrofuran. R. D. Haworth and L. Wilson, Soc. *1950*, 71.

Sulfuric acid *H_2SO_4*

Furan ring closure

s. *3*, 169; s. a. R. Kuhn and K. Dury, A. *571*, 44 (1951)

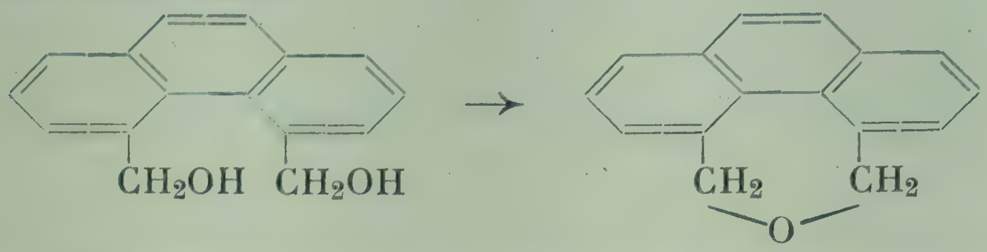
Morpholines

s. *6*, 345

Hydrochloric acid *HCl*

Cyclic ethers from diols

302/3.



Anhydrous HCl passed into a suspension of 4,5-phenanthrenedimethanol (prepn. s. 61) in benzene at room temp. for 15 min. → cyclic ether. Y: 90%. M. S. Newman and H. S. Whitehouse, Am. Soc. *71*, 3664 (1949).

Chromone ring

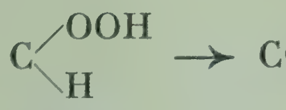
s. *1*, 546; s. a. J. S. H. Davies et al., Soc. *1950*, 3195, 3206

Hydrobromic acid *HBr*

s. *6*, 868

Ferrous sulfate *$FeSO_4$*

Ketones from hydroperoxides
Free-radical decomposition



$$C\begin{matrix}\diagup OOH\\ \diagdown H\end{matrix} \rightarrow CO$$

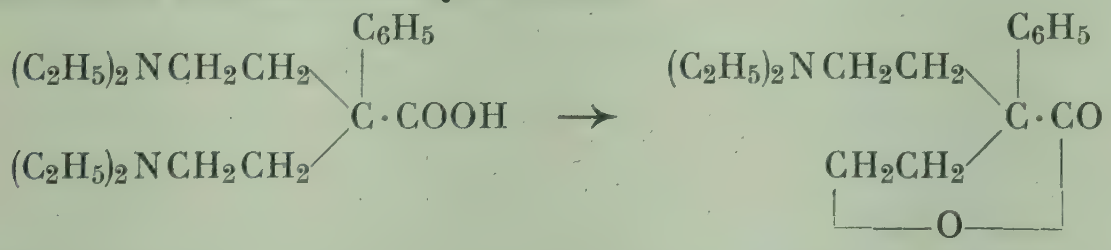
s. *1*, 246; s. a. M. S. Kharasch, A. Fono, and W. Nudenberg, J. Org. Chem. *16*, 128 (1951)

Nitrogen ↑ **OC ⇑ N**

Without additional reagents *w.a.r.*

Lactones from aminocarboxylic acids ○

304.

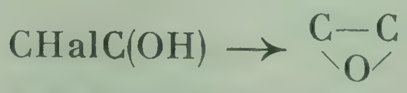


γ-N,N-Dialkylamino acids are converted on pyrolysis to γ-lactones with simultaneous elimination of dialkylamine unless decarboxylation becomes the predominating reaction.—E: α,α-Bis-(β-Diethylaminoethyl)-α-phenylacetic acid heated 30 min. at 210-222° → α-diethylaminoethyl-a-phenylbutyrolactone. Y: 84%. F. e. s. R. L. Clarke and A. Mooradian, Am. Soc. *71*, 2825 (1949).

Halogen ↑ **OC ⇑ Hal**

Sodium hydroxide *NaOH*

Oxido compounds from halogenhydrins

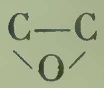


$$CHalC(OH) \rightarrow \underset{\diagdown O \diagup}{C—C}$$

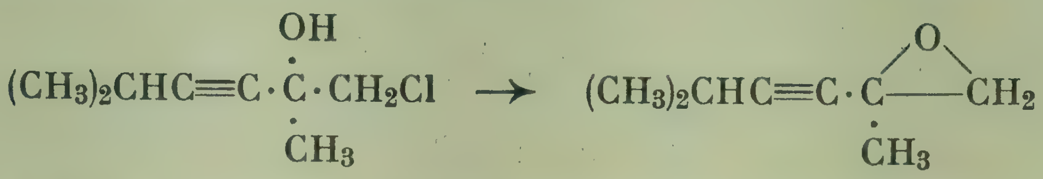
305. Iodohydroxystearic acid treated with excess cold 0.1 *N* NaOH for 1 hr. → elaidic acid oxide. Y: almost 100%.—Some dihydroxystearic acid also results when concd. alkali at 100° is used. F. e. s. G. King, Soc. *1949*, 1817.

Potassium hydroxide *KOH*

Oxido compounds from chlorohydrins

CClC(OH) →


306.

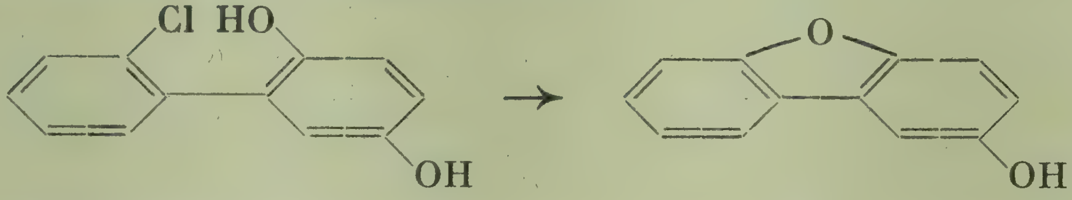


Powdered KOH added portionwise with stirring and cooling to a soln. of 2,5-dimethyl-6-chloro-3-hexyn-5-ol in abs. ether → 1,2-epoxy-2,5-dimethyl-3-hexyne. Y: 80-85%. F. Y. Perveev, Ж. *19,* 1309 (1949); f. e. s. *19,* 1303 (1949); C. A. *44,* 1008e/a.

O-Heterocyclics from halogenhydrins

○

307.

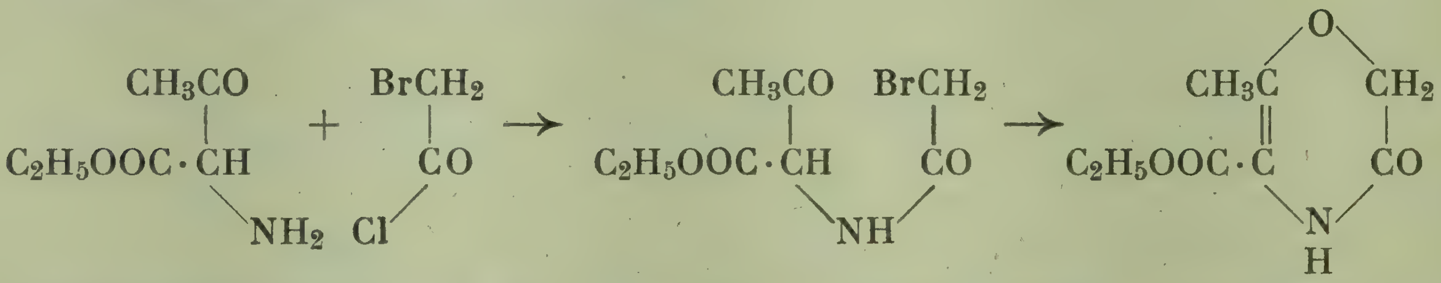


2′-Chloro-2,5-dihydroxydiphenyl heated with aq. ca. 40%-KOH and Na-hydrosulfite in an autoclave at 230° for 1 hr. → 3-hydroxydiphenylene oxide. Y: 94.5%. F. e. s. K. Schimmelschmidt, A. *566,* 184 (1950).

Sodium/alcohol *NaOR*

1,4-Oxazines
α-Halogenocarboxylic acid amides

308.

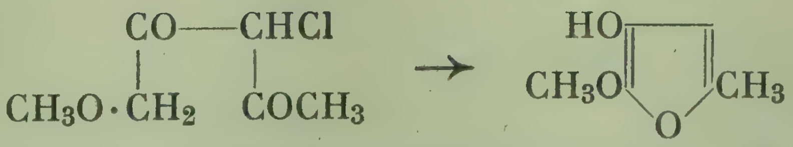


N-Methylmorpholine in dry chloroform added dropwise during 30 min. at 0° to a mixture of ethyl α-amino-β-ketobutyrate hydrochloride and α-bromoacetyl chloride in dry chloroform, and stirring continued for 1 hr. at 0° → ethyl α-bromoacetamido-β-ketobutyrate (Y: 83%) in dry ethanol treated with a soln. of Na in ethanol at 15°, and kept at this temp. for 16 hrs. → ethyl 5-hydroxy-2-methyl-1,4-oxazine-3-carboxylate (Y: 54.5%). F. e. s. G. T. Newbold, F. S. Spring, and W. Sweeny, Soc. *1950,* 909.

Potassium acetate *CH_3COOK*

Furans

309.



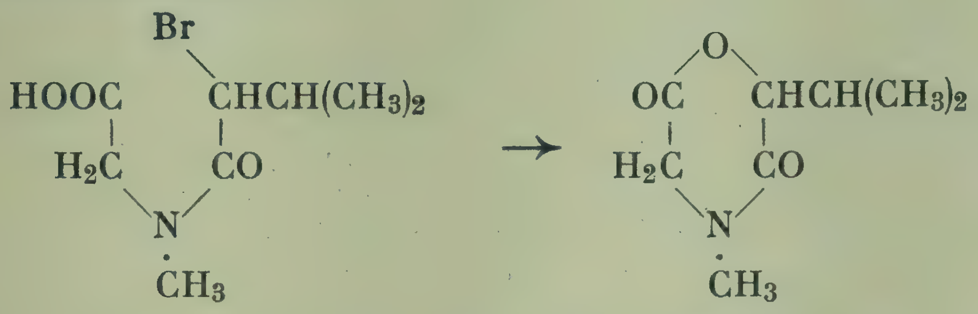
α-Chloro-γ-methoxyacetylacetone added to a soln. of K-acetate and a little acetic anhydride in glacial acetic acid, and warmed at 80° for

5 hrs. → 3-hydroxy-2-methoxy-5-methylfuran. Y: 71.4%. F. e. s. H. Henecka, Chem. B. *82*, 32 (1949).

Sodium salt *Na+*

2,5-Diketomorpholines

310.



N-α-Bromoisovalerylsarcosine dissolved in 2 *N* NaOH, evaporated to dryness in vacuo, then distilled at $150^\circ/10^{-5}$ mm. → 3,6-diketo-4-methyl-2-isopropylmorpholine. Y: 73%.—The ring is formed with varying ease depending on substitution and steric configuration. A. H. Cook and S. F. Cox, Soc. *1949*, 2347.

Via intermediates *v.i.*

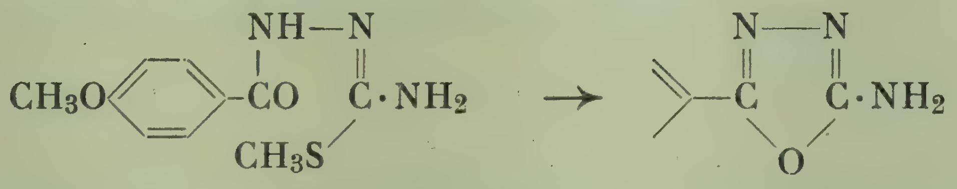
α-Bromo-γ-lactones from
α,γ-dibromocarboxylic acid bromides
s. *6*, 569

Sulfur ↑ OC ⇑ S

Without additional reagents *w.a.r.*

1,3,4-Oxadiazoles from acylthiosemicarbazides ○

311.

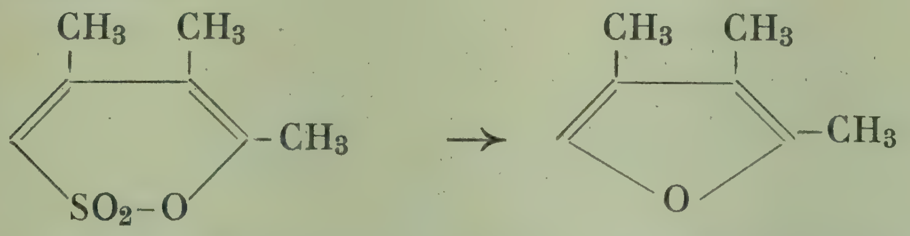


1.2 gm. p-methoxybenzoyl-S-methylisothiosemicarbazide heated ¼ hr. at 190° → 0.85 gm. 2-amino-5-p-methoxyphenyl-1,3,4-oxadiazole. F. e. s. E. Hoggarth, Soc. *1949*, 1918.

Calcium oxide/quinoline ←

Furans from sultones ←

312.

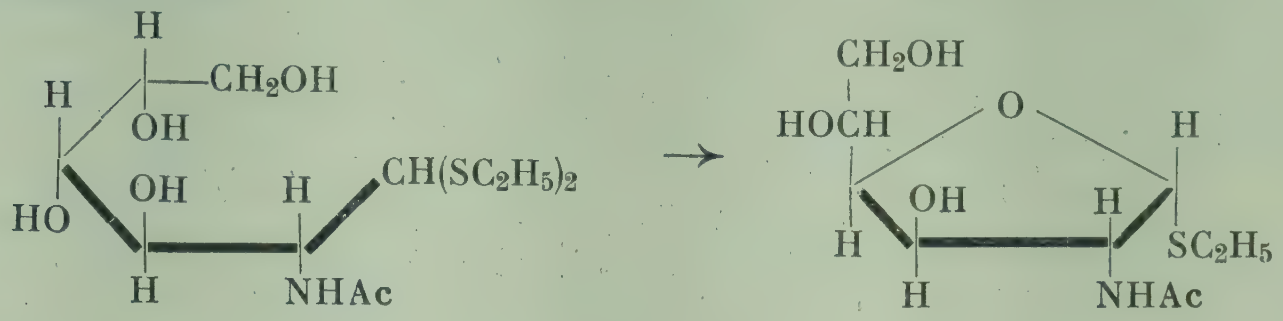


An intimate mixture of 2,3-dimethyl-4-hydroxy-1,3-pentadiene 1-sulfonic acid sultone, CaO-powder, and quinoline distilled at 200-250° → 2,3,4-trimethylfuran. Y: 76%. F. e. s. T. Morel and P. E. Verkade, R. *70*, 35 (1951).

Mercuric oxide/mercuric chloride *$HgO/HgCl_2$*

Thioglycosides ←

313.



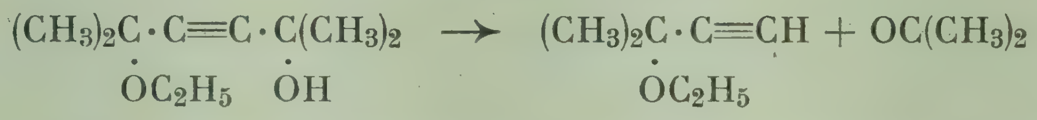
Yellow HgO added to an aq. soln. of 4.65 g. N-acetyl-D-glucosamine diethyl thioacetal, this suspension treated dropwise with vigorous stirring over a period of 20 min. an aq. soln. of $HgCl_2$, stirring maintained for 15 min. after the addition, pyridine added, and filtered → 2.01 g. ethyl 2-acetamido-2-desoxy-α-D-glucothiofuranoside. M. L. Wolfrom, S. M. Olin, and W. J. Polglase, Am. Soc. *72,* 1724 (1950).

Carbon ↑ OC ⇑ C

Potassium hydroxide *KOH*

Hydrolytic cleavage of the carbon chain
Hydrocarbons and ketones from alcohols ←

314.

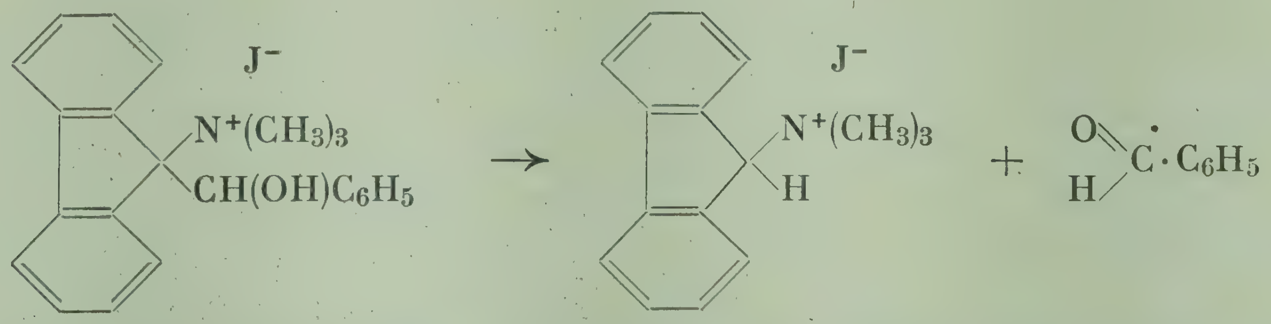


$$(CH_3)_2\underset{OC_2H_5}{\dot{C}}\cdot C\equiv C\cdot \underset{OH}{\dot{C}}(CH_3)_2 \rightarrow (CH_3)_2\underset{OC_2H_5}{\dot{C}}\cdot C\equiv CH + OC(CH_3)_2$$

A mixture of tetramethylbutynediol monoethyl ether and powdered KOH distilled → dimethylethynylcarbinol ethyl ether. Y: 71.8%. F. e. s. Y. S. Zal'kind and L. P. Chigogidze-Chanturishvili, Ж. *20,* 719 (1950); C. A. *44,* 7764h.

Sodium/alcohol *NaOR*

315.



The decomposition of certain organic alkali compounds into their components is the reason why some condensations ordinarily promoted by alkali do not occur (*83,* 110). E: Trimethyl-[9-(hydroxyphenylmethyl)-9-fluorenyl]ammonium iodide mixed with a soln. of Na in ethanol, then a little water and the equivalent amount of phenylhydrazine added → benzaldehyde phenylhydrazone (Y: 90%) and trimethyl-9-fluorenylammonium iodide (Y: 80%). G. Wittig and K. Nagel, Chem. B. *83,* 106, 110 (1950).

Red lead oxide *Pb_3O_4*

Ketones from α-hydroxycarboxylic acids ←

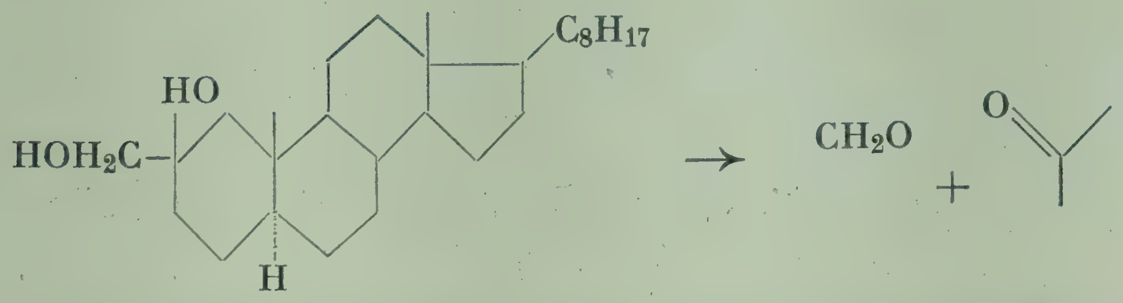
s. *6*, 901

Lead tetraacetate *$(CH_3COO)_4Pb$*

Ketones from glycols ←

Degradation

316.



200 mg. crude 2-hydroxymethyl-2-hydroxycholestane allowed to stand with Pb-tetraacetate in glacial acetic acid at 20° for 5 hrs. → 150 mg. 2-ketocholestane. F. e. s. G. Lardelli and O. Jeger, Helv. *32*, 1817 (1949); s. a. C. Dorée, J. F. McGhie, and F. Kurzer, Soc. *1949*, S167.

Oxygen *O_2*

Isatin ring ○

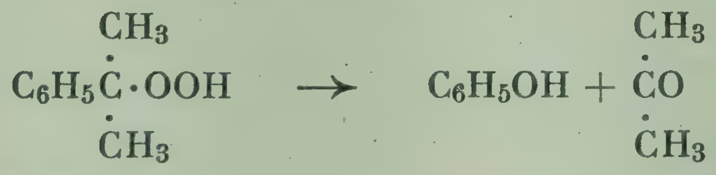
s. *6*, 775

Sulfuric acid *H_2SO_4*

Hydrolytic cleavage of the carbon chain ←

Ketones and phenols from hydroperoxides

317.



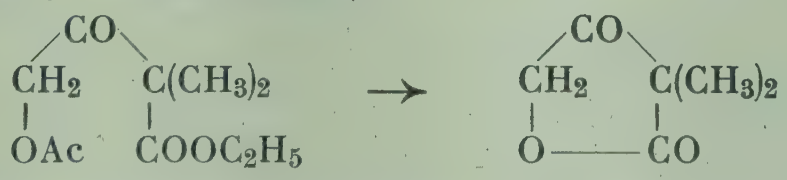
$$C_6H_5\overset{CH_3}{\underset{CH_3}{C}}\cdot OOH \longrightarrow C_6H_5OH + \overset{CH_3}{\underset{CH_3}{CO}}$$

A mixture of aq. H_2SO_4 and a soln. of isopropylbenzene hydroperoxide in isopropylbenzene refluxed 90 min. with vigorous stirring → phenol (Y: 82%) and acetone (Y: 74%). G. P. Armstrong, R. H. Hall, and D. C. Quin, Soc. *1950*, 666.

Lactones from acoxycarboxylic acid esters ○

β-Keto-γ-lactones (Tetronic acids)

318.

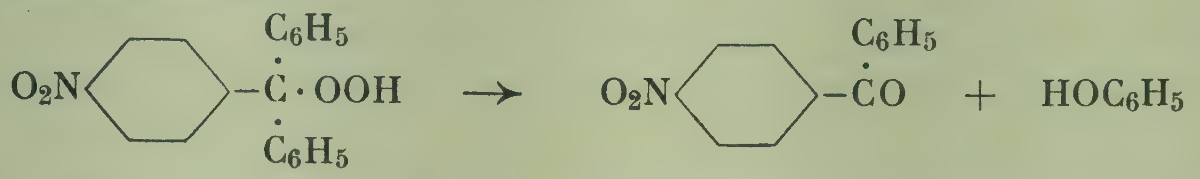


Ethyl α,α-dimethyl-γ-acetoxyacetoacetate added dropwise below 8° to rapidly stirred concd. H_2SO_4, and kept 48 hrs. in a closed container at refrigerator temp. → 3,3-dimethyltetronic acid. Y: 89.4%. F. tetronic acids s. E. B. Reid, R. B. Fortenbaugh, and H. R. Patterson, J. Org. Chem. *15*, 572 (1950).

Perchloric acid *$HClO_4$*

Hydrolytic cleavage of the carbon chain ←
Ketones and phenols from hydroperoxides
Migration aptitude

319.

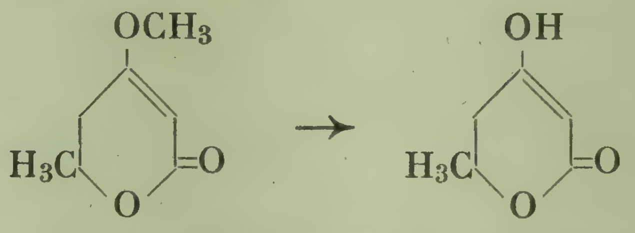


$HClO_4$ added with cooling to a soln. of p-nitrotriphenylmethyl hydroperoxide (prepn. s. 256) in glacial acetic acid, then water added → p-nitrobenzophenone. Y: 94%.—In the free-radical mechanism of thermal decomposition, the p-nitrophenyl group has a greater migration aptitude than the phenyl group. P. D. Bartlett and J. D. Cotman, Jr., Am. Soc. *72*, 3095 (1950); s. a. M. S. Kharasch et al., J. Org. Chem. *15*, 775, 748 (1950); free-radical mechanism s. J. Org. Chem. *15*, 753, 763 (1950).

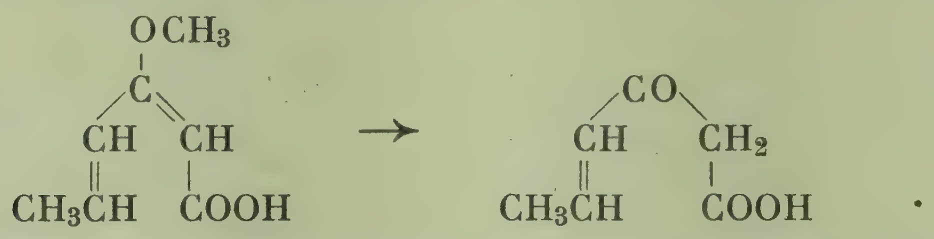
Hydrochloric acid *HCl*

Hydrolysis of enolethers ←
Ketones and enols from enolethers

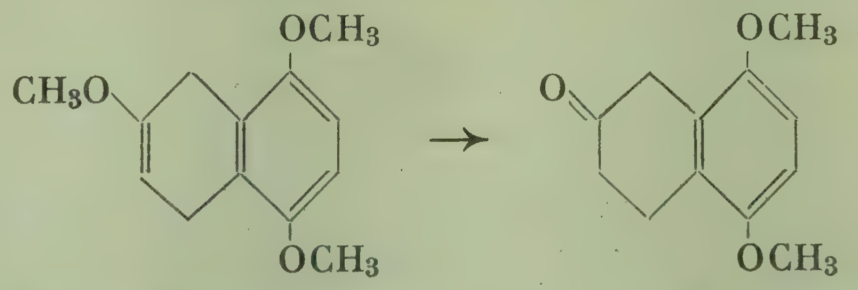
320.



An ethereal soln. of 4-methoxy-6-methyl-5,6-dihydro-2-pyrone treated with a carefully controlled quantity of concd. HCl, and kept at 20° for 48 hrs. with occasional stirring → 4-hydroxy-6-methyl-5,6-dihydro-2-pyrone. Y: 75%. E. R. H. Jones and M. C. Whiting, Soc. *1949*, 1419; with HI s. E. B. Reid and W. R. Ruby, Am. Soc. *73*, 1054 (1951).



Concd. HCl added at 0° to a suspension of β-methoxysorbic acid in dry ether, and kept 2.5 hrs. at the same temp. with occasional shaking → crotonylacetic acid. Y: 80%. Soc. *1949*, 1419.

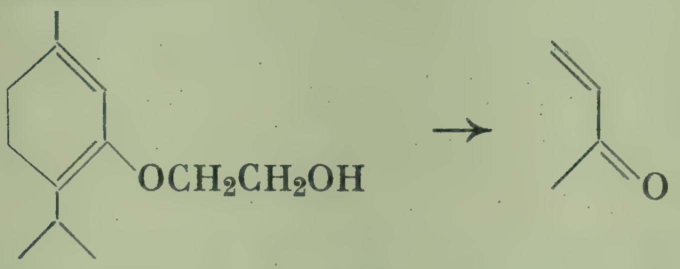


2 *N* HCl added dropwise to an alc. soln. of 1,4,6-trimethoxy-5,8-dihydronaphthalene, and most of the alcohol distilled off in vacuo at 30°

→ 5,8-dimethoxy-2-tetralone. Y: almost 100%. C. A. Grob and H. Wicki, Helv. *31*, 1706 (1948).

Ketones from enolethers

321.



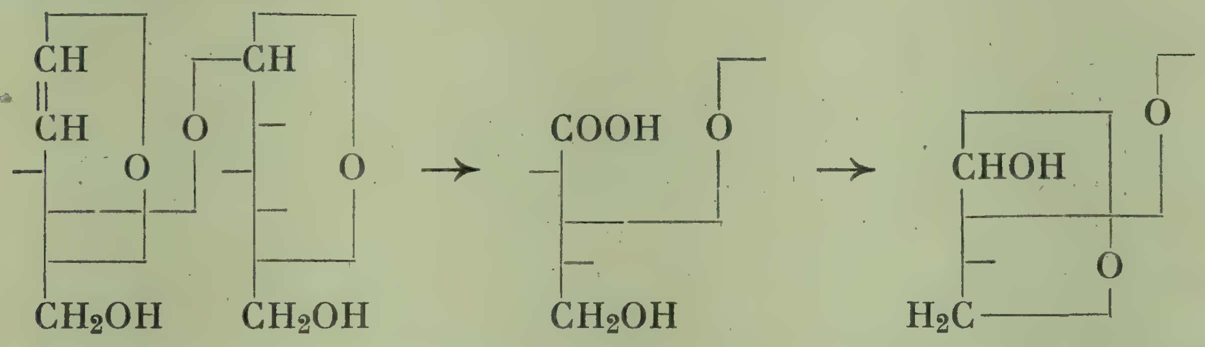
17.5 gm. 2-(2-hydroxyethoxy)-4-methyl-1-isopropyl-1,4-cyclohexadiene refluxed 20 min. with 5%-HCl → 14 gm. piperitone.—Because of the high boiling point of hydroxylated ethers compared with that of the ketone produced, the latter can be readily purified by distillation. F. e. s. A. J. Birch and S. M. Mukherji, Soc. *1949*, 2531.

Ferric sulfate/hydrogen peroxide/barium carbonate *$Fe_2(SO_4)_3/H_2O_2/BaCO_3$*

Ruff degradation of carbohydrates
Elimination of carbon monoxide ←

Degradation of glycals via aldonic acids

322.

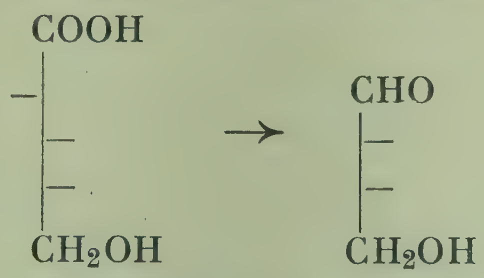


Maltal in aq. K-carbonate treated slowly at 30-50° with 4%-$KMnO_4$ until the color persists, and the product isolated as Ca salt → Ca glucosido-3-arabonate (Y: 60%) boiled 10 min. with Ba-carbonate and $Fe_2(SO_4)_3$ in water, filtered, cooled, the stirred soln. treated with 30%-H_2O_2 followed by an additional portion after 3 hrs., and warmed gently on a water bath → glucosido-2-erythrose (Y: 79%). A. M. Gakhokidze, Ж. *20*, 116 (1950); f. e. s. Ж. *20*, 120, 289; C. A. *44*, 5819c/g, 6822c.

Ferric sulfate/hydrogen peroxide/barium acetate *$Fe_2(SO_4)_3/H_2O_2/(CH_3COO)_2Ba$*

Aldehydes from α-hydroxycarboxylic acids

323.



Ca-D-arabonate slowly added to a gently boiling aq. soln. of Ba-acetate and $Fe_2(SO_4)_3$, boiling continued for 20 min., filtered through a carbon pad, H_2O_2 added in 2 portions at 40°, and allowed to stand overnight → D-erythrose. Y: 46%. W. G. Overend, M. Stacey, and L. F. Wiggins, Soc. *1949*, 1358; method, see Hockett and Hudson, Am. Soc. *56*, 1632 (1934); s. a. Am. Soc. *72*, 4546 (1950).

Formation of N—N Bond

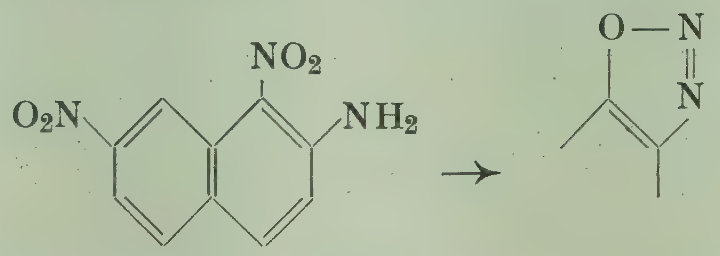
Rearrangement

Nitrogen/Carbon Type NN ↶ NC

Sodium nitrite *$NaNO_2$*

Diazo oxides from o-nitramines ○

324.



A soln. of 0.5 gm. 1,7-dinitro-2-naphthylamine in H_2SO_4 (d. 1.84) treated below 10° with a soln. of $NaNO_2$ in H_2SO_4 (d. 1.84), and the mixture stirred into a suspension of Cu-carbonate in glacial acetic acid → 0.45 gm. 7-nitronaphthalene-2,1-diazo oxide. H. H. Hodgson and R. E. Dean, Soc. *1950*, 818.

Exchange

Hydrogen ↑ NN ⇅ H

Sodium acetate *CH_3COONa*

Azo compounds by coupling N:N

s. *6*, 325

Sodium nitrite *$NaNO_2$*

Triazenes ←

s. *1*, 607; s. a. D. E. Pearson, W. C. Holland, and H. P. Midgett, Am. Soc. *72*, 2303 (1950)

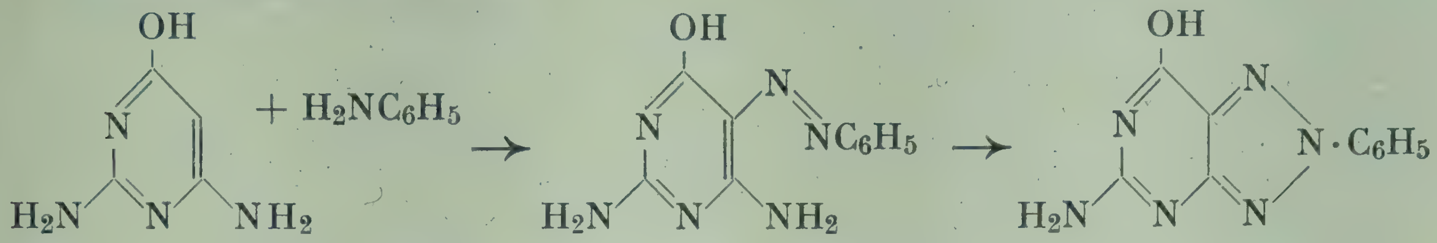
1,2,3-Triazoles ○

s. *1*, 262-4; s. a. K. Eiter and A. Nezval, M. *81*, 404 (1950)

Cupric sulfate *$CuSO_4$*

1,2,3-Triazole ring via azo compounds
v-Triazolo(d)pyrimidines

325.

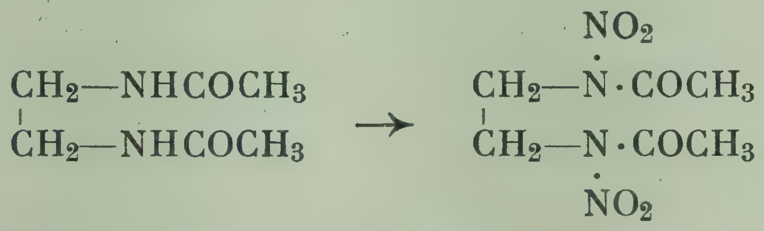


Aniline in HCl diazotized with aq. $NaNO_2$ below 3°, excess HNO_2 destroyed with urea, the diazonium salt soln. so obtained added slowly to a stirred soln. of 2,4-diamino-6-hydroxypyrimidine sulfate in aq. Na-acetate, and stirred for 10 min. → 2,4-diamino-5-phenylazo-6-hydroxypyrimidine sesquihydrate (Y: ca. 100%) added to a refluxing mixture of $CuSO_4$, water, and pyridine, and refluxing continued for 3 hrs. with vigorous stirring → 2-phenyl-5-amino-7-hydroxy-v-triazolo(d)pyrimidine (Y: 70.5%). F. e. s. F. R. Benson, L. W. Hartzel, and W. L. Savell, Am. Soc. *72,* 1816 (1950).

Acetic anhydride *$(CH_3CO)_2O$*

Nitration $N·NO_2$
Nitramines

326.



$$\begin{array}{l} CH_2\text{—}NHCOCH_3 \\ | \\ CH_2\text{—}NHCOCH_3 \end{array} \rightarrow \begin{array}{l} \qquad\quad NO_2 \\ CH_2\text{—}N\cdot COCH_3 \\ | \\ CH_2\text{—}N\cdot COCH_3 \\ \qquad\quad NO_2 \end{array}$$

A mixture of acetic anhydride and 98%-HNO_3 may be able to nitrate compounds which remain unchanged in 98%-HNO_3 alone or mixed with concd. H_2SO_4.—E: Ethylenebisacetamide added portionwise below 5° to the above mixture, and worked up after 6 hrs. at 5° → N,N′-dinitroethylenebisacetamide. Y: 83%. F. e. s. W. E. Bachmann et al., Am. Soc. *72,* 3132 (1950); s. a. A. F. McKay and J. E. Milks, Am. Soc. *72,* 1616 (1950).

Stannous chloride *$SnCl_2$*

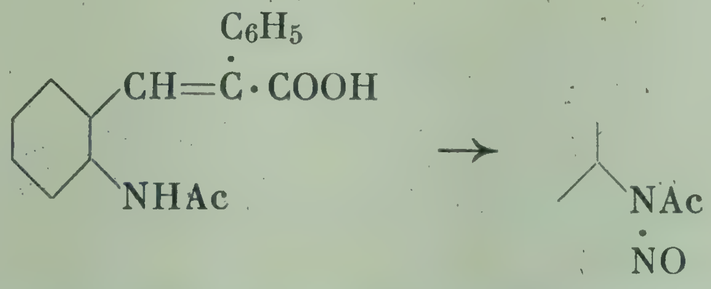
Hydrazines from amines $NH_2 \rightarrow NHHN_2$

s. *2,* 304; s. a. P. P. T. Sah, R. *69,* 1025 (1950)

Nitrosyl chloride *NOCl*

N-Nitrosamines N·NO

327.



A soln. of NOCl in glacial acetic acid added dropwise at 0° with stirring to a mixture of 5 gm. o-acetamido-α-phenylcinnamic acid, freshly fused

K-acetate, P_2O_5, glacial acetic acid, and acetic anhydride, then stirred for a further 30 min. → 4.47 gm. o-nitrosoacetamido-α-phenylcinnamic acid. D. H. Hey and J. M. Osbond, Soc. *1949*, 3164; f. e. s. Soc. *1949*, 3181.

Sulfur dioxide *SO_2*

Hydrazines from amines $NH_2 \rightarrow NHNH_2$

s. *1*, 261; s. a. R. L. Barker et al., J. Soc. Chem. Ind. *68*, 277 (1949)

Hydroxylamine-O-sulfonic acid *NH_2OSO_3H*

Hydrazines from amines $NH_2 \rightarrow NHNH_2$

328. $n\text{-}C_4H_9NH_2 + HSO_3ONH_2 \rightarrow n\text{-}C_4H_9NHNH_2$

An aq. soln. of hydroxylamine-O-sulfonic acid added dropwise over a period of 8 min. to a refluxing mixture of n-butylamine and water, cooled, acidified with glacial acetic acid, warmed 10 min. to 50° with benzaldehyde, cooled, extracted with ether, added to aq. oxalic acid, and steam-distilled until no more benzaldehyde comes over → n-butylhydrazine oxalate. Y: 60%. F. e., with lower yields, s. G. Gever and K. Hayes, J. Org. Chem. *14*, 813 (1949).

Chlorine ion *Cl^-*

N-Nitramines $N \cdot NO_2$

s. *4*, 290; s. a. Am. Soc. *72*, 341 (1950)

Oxygen ↑ NN ⇅ O

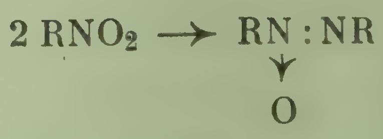
Zinc *Zn*

Sym. azo compounds from nitro compounds $2\,RNO_2 \rightarrow RN{:}NR$

s. *3*, 251; s. a. R. B. Carlin and W. O. Forshey, Jr. Am. Soc. *72*, 793 (1950)

Arsenic trioxide *As_2O_3*

Azoxy compounds from nitro compounds



$2\,RNO_2 \rightarrow RN{:}\underset{\overset{\downarrow}{O}}{N}R$

s. *4*, 292; s. a. R. Gaudry and K. F. Keirstead, Can. J. Research *27 B*, 890 (1949)

Elimination

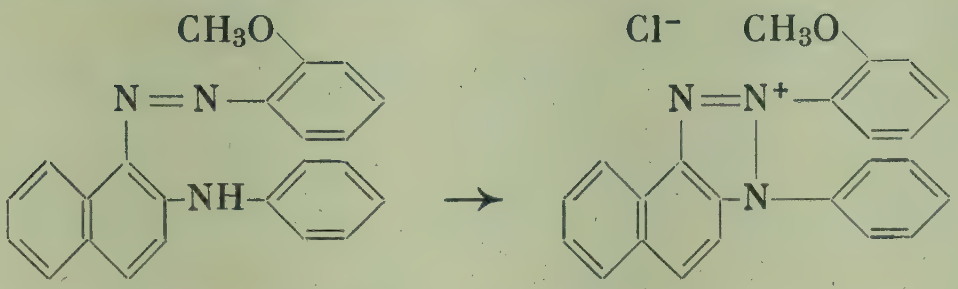
Hydrogen ↑ **NN ⇑ H**

Alkyl nitrite *RONO*

1,2,3-Triazolium salts from o-aminoazo compounds ○

Tetrazolium salts from formazans

329.



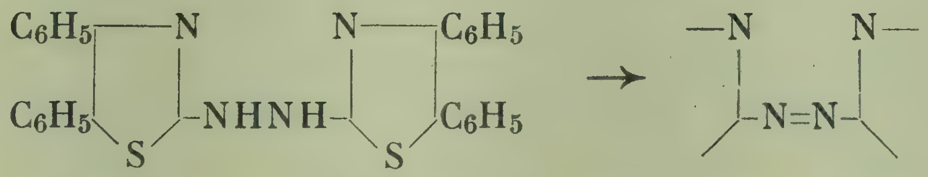
5 gm. o-methoxybenzeneazo-N-phenyl-β-naphthylamine in chloroform dehydrogenated with isoamyl nitrite and HCl-gas → 6.8 gm. 2-phenyl-3-(o-methoxyphenyl)-3*H*-naphtho[1,2]triazolium chloride. F. e., also with $K_2Cr_2O_7$, s. R. Kuhn and E. Ludolphy, A. *564*, 35 (1949); tetrazolium salts from formazans s. D. Jerchel and H. Fischer, A. *563*, 200, 208 (1949); S. W. Fox and E. Hemmingson Atkinson, Am. Soc. *72*, 3629 (1950).

Nitric acid *HNO_3*

Azo compounds from hydrazo compounds ·NHNH· → ·N:N·

s. *6,* 869

330.



Azothiazoles. A suspension of 4,4′,5,5′-tetraphenylhydrazothiazole-2,2′ in dil. HNO_3 gradually heated until the material suddenly turns deep red → 4,4′,5,5′-tetraphenylazothiazole-2,2′. Y: ca. 100%. F. e. s. H. Beyer et al., Chem. B. *82*, 148, cf. 143 (1949).

Formation of N—S Bond

Uptake

Addition to Sulfur and Carbon **NS ⇓ SC**

Sodium hydroxide *NaOH*

Dithiocarbamic acids from amines NH → NCSSH

s. *6,* 332

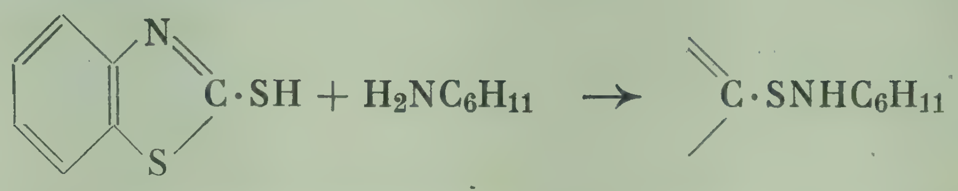
Exchange

Hydrogen ↑ NS ⇅ H

Chlorine *Cl*

Sulfenamides from amines NH → NSR

331.

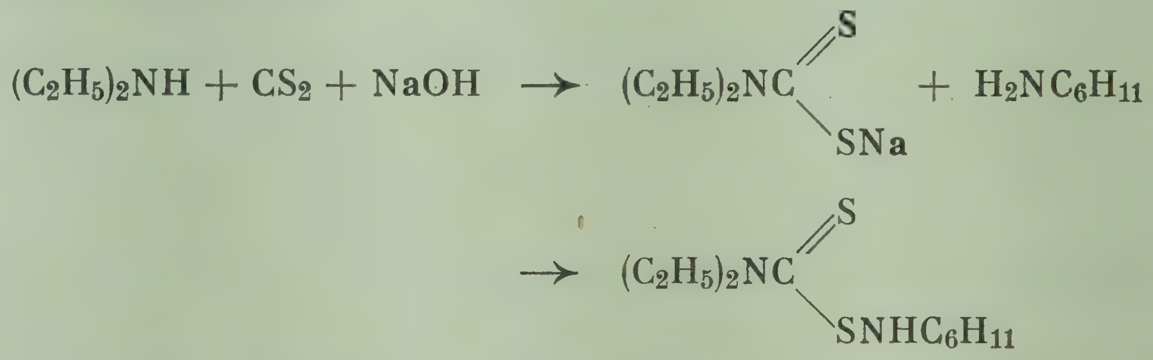


A mixture of Cl_2 and air introduced at 25-32° and a pH of 13.1-12.5 to a rapidly stirred aq. soln. of benzothiazole-2-thiol, NaOH, and cyclohexylamine over a period of 4-5 hrs. → N-cyclohexylbenzothiazole-2-sulfenamide. Y: 96.5%. F. e. and methods s. E. L. Carr, G. E. P. Smith, and G. Alliger, J. Org. Chem. *14*, 921 (1949).

Iodine *I*

Thiocarbamylsulfenamides from amines via dithiocarbamic acids ←

332.



$$(C_2H_5)_2NH + CS_2 + NaOH \rightarrow (C_2H_5)_2NC\begin{matrix} \nearrow S \\ \searrow SNa \end{matrix} + H_2NC_6H_{11} \rightarrow (C_2H_5)_2NC\begin{matrix} \nearrow S \\ \searrow SNHC_6H_{11} \end{matrix}$$

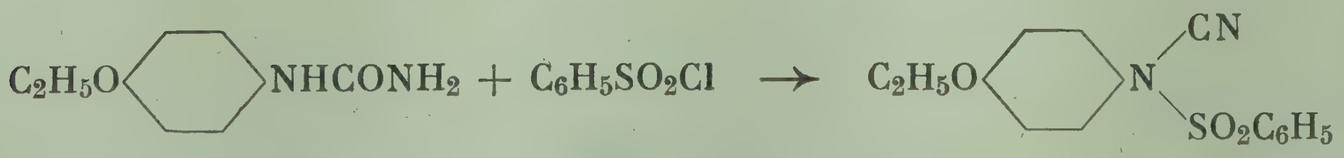
Cyclohexylamine added to a soln. of Na-N,N-diethyldithiocarbamate, prepared from diethylamine, CS_2, and NaOH in water, then an aq. soln. of iodine and KI slowly added at 15-31° over a period of 1.5 hrs. → N,N-diethylthiocarbamyl-N-cyclohexylsulfenamide. Y: 82%. F. e. and methods s. G. E. P. Smith et al., J. Org. Chem. *14*, 935 (1949).

Halogen ↑ NS ⇅ Hal

Pyridine *C_5H_5N*

N-Sulfonylcyanamides from ureas ←

333.



By treating a soln. or suspension of a subst. arylurea in pyridine with a sulfonyl chloride below 60°, and working up after 12-15 min., N-sulfonylcyanamides are obtained. The velocity of the reaction is affected noticeably by the choice of the sulfonyl chloride.—E: p-Ethoxyphenylurea and benzenesulfonyl chloride → benzenesulfonyl-p-ethoxyphenylcyanamide. Y: 80%. F. e. s. F. Kurzer, Soc. *1949*, 3029.

Elimination

Hydrogen NS ⇑ H

Iodine *I*

Tetrahydro-1,2,5-thiadiazine-6-thiones from amino-dithiocarbamic acids ○

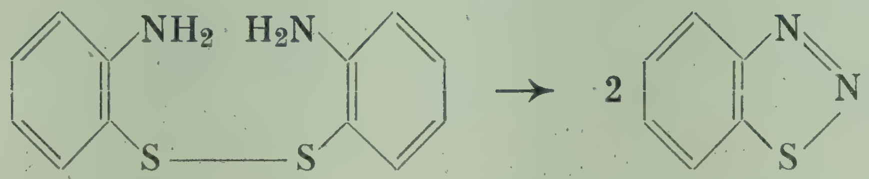
s. *6*, 363

Sulfur NS ⇑ S

Cuprous chloride *CuCl*

1,2,3-Benzothiadiazoles from 0,0′-diaminodisulfides ○

334.



An ice-cold soln. of 2,2-diaminodiphenyl disulfide in concd. H_2SO_4 slowly added during ca. 30 min. to nitrosylsulfuric acid (from $NaNO_2$ and concd. H_2SO_4) kept in a freezing mixture, the tetrazonium salt soln. so obtained poured into an ice-cold soln. of CuCl in concd. HCl, then NaOH added → 1,2,3-benzothiadiazole. Y: 85%. F. reactions of the tetrazonium salt s. A. Burawoy and C. Turner, Soc. *1950*, 469.

Formation of N—Rem Bond

Exchange

Oxygen ↾ NRem ⥮ O

Without additional reagents *w.a.r.*

Organo lead compounds ←

N-(Trialkylplumbi)sulfonamides

335. $(CH_3CH_2CH_2)_3PbOH + H_2NSO_2C_6H_5 \rightarrow (CH_3CH_2CH_2)_3PbNHSO_2C_6H_5$

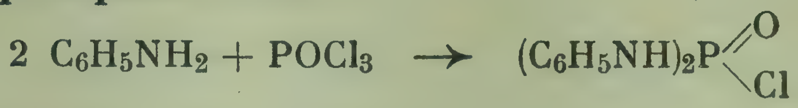
An alc. soln. of benzenesulfonamide added to an alc. soln. of tri(n-propyl)-Pb hydroxide, and water added after 10 min. → N-(tri-n-propylplumbi)benzenesulfonamide. Y: almost 100%. F. e. s. B. C. Saunders, Soc. *1950*, 684.

Halogen ↑ NRem ⇅ Hal

Without additional reagents *w.a.r.*

Diaminochlorophosphine oxides ←

336.



$$2\ C_6H_5NH_2 + POCl_3 \rightarrow (C_6H_5NH)_2P(=O)Cl$$

An ethereal soln. of aniline added slowly to an ice-cooled ethereal soln. of the calculated quantity of $POCl_3$, and allowed to stand overnight → dianilinochlorophosphine oxide. Y: almost 100%. F. e. s. H. G. Cook et al., Soc. *1949*, 2921.

Silver and lead salts *Ag^+ and Pb^{++}*

Silyl isocyanates and isothiocyanates ←

337. $$(C_6H_5)_3SiCl + AgNCO \rightarrow (C_6H_5)_3SiNCO$$

Triphenylsilyl chloride and Ag-isocyanate refluxed 1 hr. in benzene under N_2 → triphenylsilyl isocyanate. Y: 82-85%.—Similarly with Pb-isothiocyanate: Triphenylsilyl isothiocyanate. Y: 97%. F. methods s. H. Gilman, B. Hofferth, and H. W. Melvin, Am. Soc. *72*, 3045 (1950).

Remaining elements ↑ NRem ⇅ Rem

Without additional reagents *w.a.r.*

Aminoboranes ←

338. $$B_2H_6 + 2\,(CH_3)_2NH \rightarrow [B_2H_6 \cdot 2\,(CH_3)_2NH] \rightarrow (CH_3)_2NBH_2$$

Diborane passed into dry liq. dimethylamine at —42°, the excess dimethylamine pumped off in a high vacuum at room temp., dry N_2 admitted to bring the pressure to 400 mm., and the addition compound obtained heated at 130° with sublimation of the reaction product → dimethylaminoborane. Y: ca. 100%. F. e. s. A. B. Burg and C. L. Randolph, Jr., Am. Soc. *71*, 3451 (1949).

Formation of N—C Bond

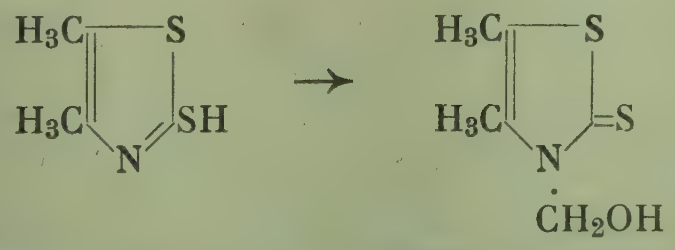
Uptake

Addition to Oxygen and Carbon NC ⇓ OC

Without additional reagents *w.a.r.*

N-Hydroxymethylation ←

339.

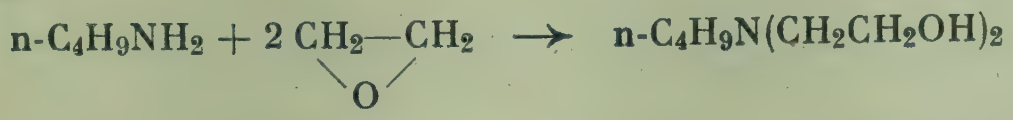


4,5-Dimethyl-2-mercaptothiazole and 37%-formaldehyde agitated and heated together at 93-95° for 2 hrs. → 3-hydroxymethyl-4,5-dimethyl-

2-thiono-4-thiazoline. Y: 89%. F. D. Stewart and R. A. Mathes, J. Org. Chem. *14*, 1111 (1949).

Di(hydroxyalkyl)amines from oxido compounds ←

340.

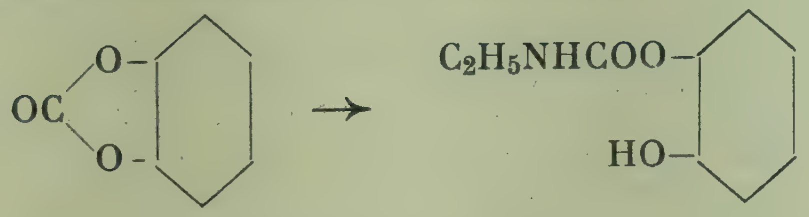


$$n\text{-}C_4H_9NH_2 + 2\,CH_2\text{—}CH_2 \rightarrow n\text{-}C_4H_9N(CH_2CH_2OH)_2$$

1.21 moles ethylene oxide bubbled into a stirred aq. soln. of 0.526 mole n-butylamine over a period of 6.5 hrs. → bis-(β-hydroxyethyl)-n-butylamine. Y: 85%. F. e. s. A. F. McKay and H. H. Brownell, J. Org. Chem. *15*, 648 (1950); s. a. J. Lecocq, Bl. *1950*, 188.

Hydroxyurethans from carbonic acid esters C

341.



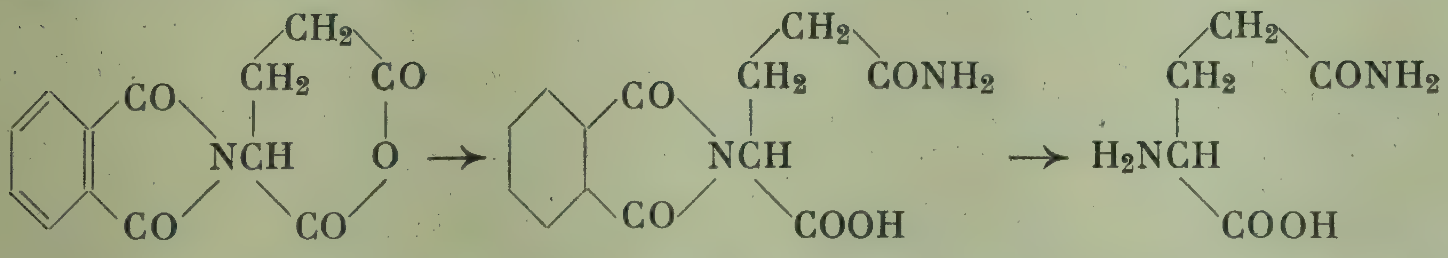
A soln. of ethylamine in alcohol-water added to a suspension of 40.8 gm. pyrocatechol carbonate in ice-cold alcohol → 35 gm. pyrocatechol mono(ethylcarbamate) (startg. m. f. 504). F. e. s. S. Petersen, A. *562*, 205 (1949).

Dicarboxylic acid monoamides from dicarboxylic acid anhydrides

s. *4*, 308; s. a. R. Adams and J. B. Campbell, Am. Soc. *72*, 128, 153 (1950); G. A. Swan, Soc. *1950*, 1534

Glutamines
Prim. amines from phthalimides; mild hydrolysis in the cold

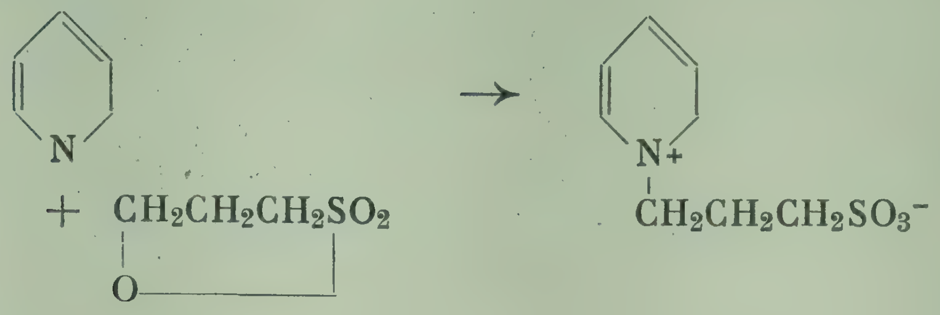
342.



A soln. of phthalyl-L-glutamic anhydride in dioxane treated with small quantities of dry ethereal NH_3 in excess, and worked up when the precipitation is complete → phthalyl-L-glutamine (Y: 77%) dissolved in aq. Na-carbonate, treated with 50%-hydrazine hydrate, and allowed to stand at room temp. for 2 days → L-glutamine (Y: 67%).—The phthalyl derivative differs from the carbobenzoxy derivative in combining with ammonia and amines to form γ-amides instead of α-amides. F. e., also N-subst. glutamines, s. F. E. King and D. A. A. Kidd, Soc *1949*, 3315.

Aminosulfonic acid inner salts from sultones

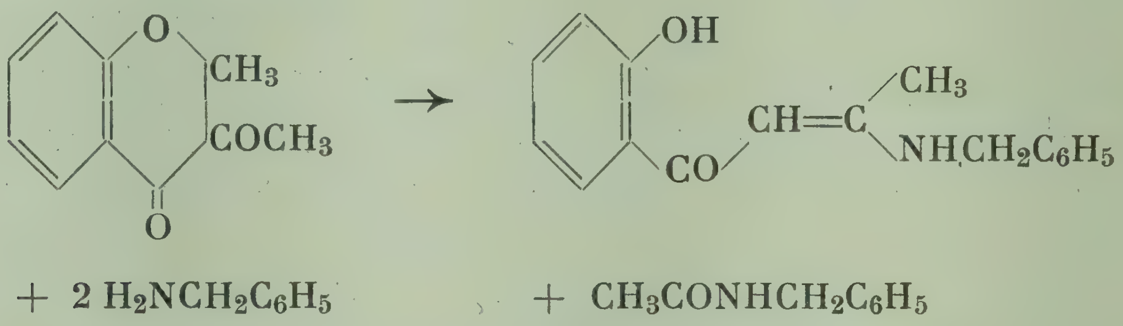
343.



Propane sultone dissolved in pyridine, and heated 1 hr. on a water bath after the initial vigorous reaction has subsided → 1-(N-pyridyl)-propane sulfonic acid betaine. Y: ca. 100%. F. e. and adducts of sultones s. J. H. Helberger, G. Manecke, and R. Heyden, A. *565*, 22 (1949).

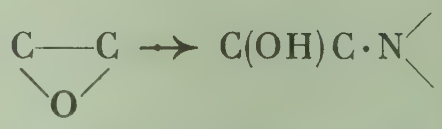
Chromone ring opening

344.



A soln. of 3-acetyl-2-methylchromone and benzylamine in benzene allowed to stand at room temp. for 24 hrs. → 2-β-benzylaminocrotonylphenol (Y: ca. 90%) and acetobenzylamide (Y: ca. 100%) (*1949*, 2142).—Treatment of 3-aroylflavones with benzylamine results in all cases in the loss of the 3-aroyl group as an aroylbenzylamide and formation of an unsatd. benzylamino compound; this general reaction may be used for orientation purposes (*1950*, 2759). F. e. s. W. Baker, V. S. Butt, and F. Glockling, Soc. *1949*, 2142; *1950*, 2759.

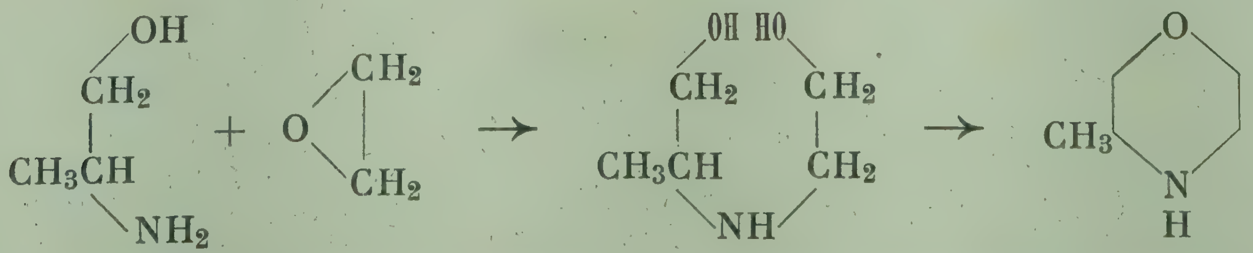
N-Subst. aminoalcohols from oxido compounds



$C{-}C$ (with bridging O) $\rightarrow C(OH)C{\cdot}N<$

s. *1*, 277/8; *2*, 317/8; *3*, 362; s. a. N. G. Barker and N. H. Cromwell, Am. Soc. *73*, 1051 (1951)

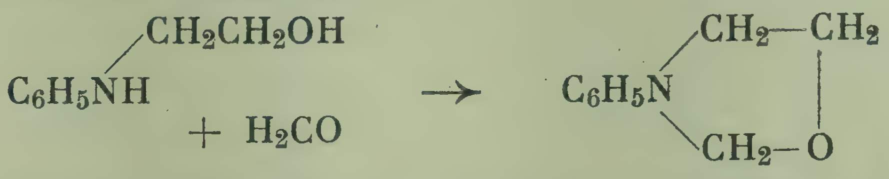
345.



Morpholines. Ethylene oxide in alcohol added with cooling and stirring to β-hydroxyisopropylamine in alcohol → α-methyl-β,β′-dihydroxydiethylamine (Y: 95%) heated with concd. H_2SO_4 (d. 1.84) at 170–180° for 8 hrs., and isolated as hydrochloride → 3-methylmorpholine hydrochloride (Y: 93%).—The reaction with olefin oxides proceeds as well in abs. as in moist alcohol, i. e. 95%-ethanol.—F. e. s. A. Y. Berlin and T. P. Sycheva, Ж. *20,* 640 (1950); C. A. *44,* 7853f.

Oxazolidines from aminoalcohols ○

346.



(β-Hydroxyethyl)aniline rubbed with excess 40%-formaldehyde until, after 1-2 min., a clear soln. is formed → 3-phenyloxazolidine. Y: ca. 100%. F. e. s. G. A. R. Kon and J. J. Roberts, Soc. *1950,* 978; s. a. L. H. Goodson and H. Cristopher, Am. Soc. *72,* 358 (1950); E. L. Engelhardt, F. S. Crossley, and J. M. Sprague, Am. Soc. *72,* 2718 (1950); s. a. L. W. Daasch and U. E. Hanninen, Am. Soc. *72,* 3673 (1950).

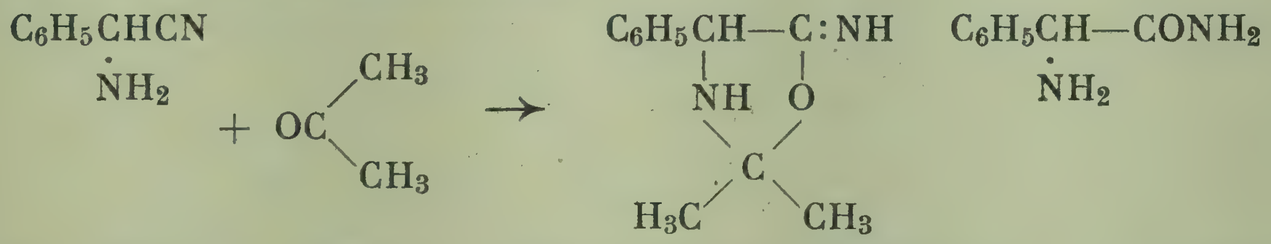
Oxazolidines from cyanohydrin acetates

s. *6,* 73

Sodium/alcohol *NaOR*

α-Aminocarboxylic acid amides from α-aminonitriles via oxazolidines ←

347.

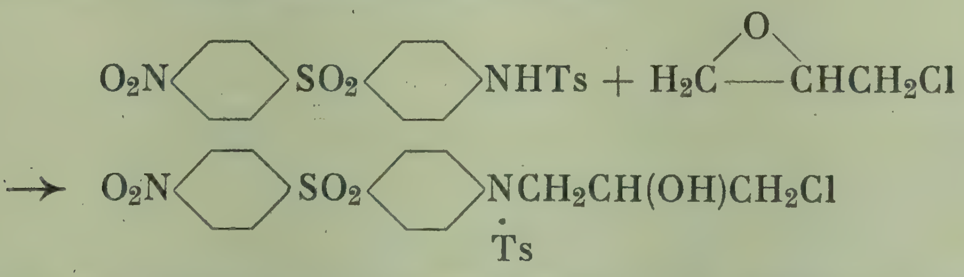


A soln. of Na in methanol added to a soln. of 20 gm. α-aminobenzyl cyanide in cold acetone → 23 gm. 5-imino-4-phenyl-2,2-dimethyloxazolidine, 15 gm. of which refluxed with water → 13 gm. α-aminophenylacetamide. J. D. Billimoria and A. H. Cook, Soc. *1949,* 2323.

Pyridine *C_5H_5N*

Aminoalcohols from oxido compounds ↺

348.

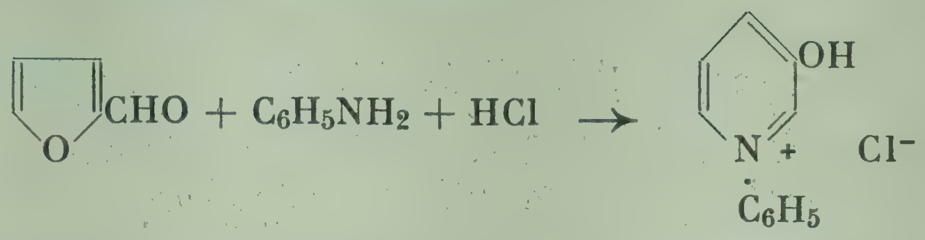


A mixture of 4-tosylamino-4′-nitrodiphenyl sulfone, pyridine, and epichlorohydrin heated on a steam bath for 1 hr. → 4-(N-tosyl-γ-chloro-β-hydroxypropylamino)-4′-nitrodiphenyl sulfone. Y: 85%. F. e. s. B. R. Baker, M. V. Querry, and A. F. Kadish, J. Org. Chem. *15,* 402 (1950).

Hydrochloric acid *HCl*

Ring enlargement ←
N-Heterocyclics from O-heterocyclics

349.

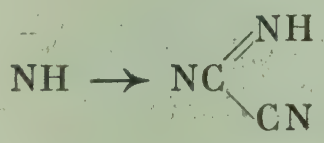


Furfural in alcohol added at 15° to a soln. of aniline and concd. HCl in alcohol, kept in an ice-bath for 3 hrs., steam-distilled, and the residue worked up → 1-phenyl-3-hydroxypyridinium chloride. Y: 49%. C. F. Koelsch and J. J. Carney, Am. Soc. *72*, 2285 (1950).

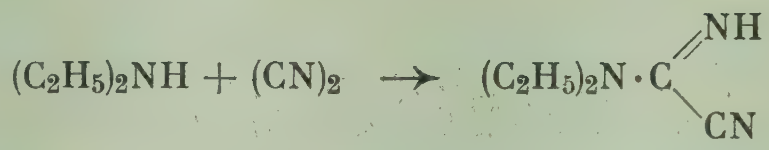
Addition to Nitrogen and Carbon NC ⇓ NC

Without additional reagents *w.a.r.*

Cyanoformamidines from amines



350.

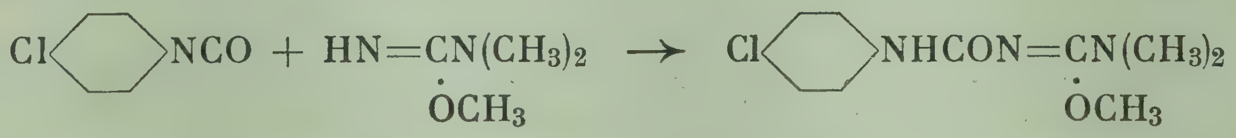


$(C_2H_5)_2NH + (CN)_2 \rightarrow (C_2H_5)_2N\cdot C(=NH)CN$

A soln. of diethylamine in anhydrous ethyl acetate cooled in an ice-bath, and saturated with cyanogen → N-diethylcyanoformamidine. Y: 70%. F. e. s. H. M. Woodburn, B. A. Morehead, and W. H. Bonner, J. Org. Chem. *14*, 555 (1949).

Isobiurets from isoureas ←

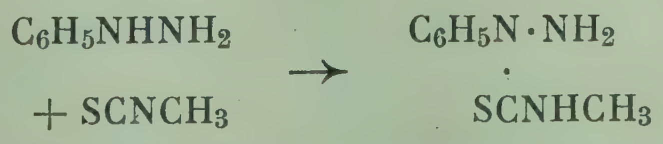
351.



A soln. of 7.5 gm. O,N,N-trimethylisourea in dry ether added to a soln. of 10 gm. p-chlorophenyl isocyanate in dry ether, and worked up after a few min. → 10.25 gm. 1-(p-chlorophenyl)-4,5,5-trimethyl-4-isobiuret. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, Soc. *1949*, 1732.

Thiosemicarbazides from isothiocyanates and hydrazines ←

352.

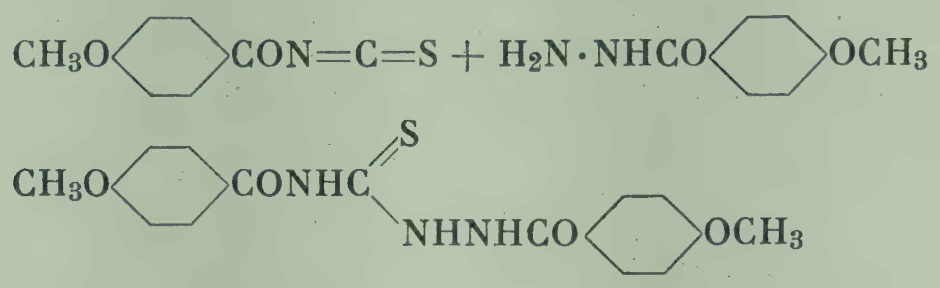


$C_6H_5NHNH_2 + SCNCH_3 \rightarrow C_6H_5N(SCNHCH_3)\cdot NH_2$

A soln. of 1.3 gm. methyl isothiocyanate and 1.9 gm. phenylhydrazine in ethanol warmed for several min., then evaporated under reduced pressure → 2 gm. 2-phenyl-4-methylthiosemicarbazide. J. S. Elvidge and F. S. Spring, Soc. *1949*, S135; s. a. J. Druey and B. H. Ringier, Helv. *34*, 195 (1951); cf. J. D. Brooks et al., Soc. *1950*, 452; in aq. soln. s. E. Schmidt et al., A. *568*, 192 (1950).

Acylthiosemicarbazides from acylisothiocyanates ←

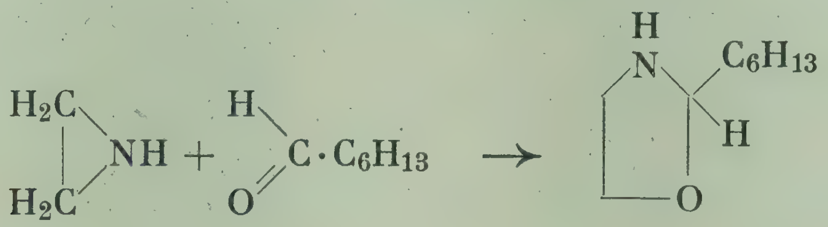
353.



1.9 gm. p-methoxybenzoyl isothiocyanate (prepn. s. 480) added during 5 min. to a stirred soln. of 1.7 gm. p-methoxybenzoylhydrazide in warm alcohol, and worked up after 1 hr. → 2.8 gm. 1,4-di-p-methoxybenzoylthiosemicarbazide. F. e. s. E. Hoggarth, Soc. *1949*, 1160.

Oxazolidines from oxo compounds ←

354.



Ethyleneimine added dropwise at 5-10° over a period of 1.5-2 hrs. to a soln. of heptaldehyde in ethyl or isopropyl ether, and refluxed ca. 24 hrs. → 2-hexyloxazolidine. Y: 95%. F. e., with lower yields, s. J. B. Doughty, C. L. Lazzell, and A. R. Collett, Am. Soc. *72*, 2866 (1950).

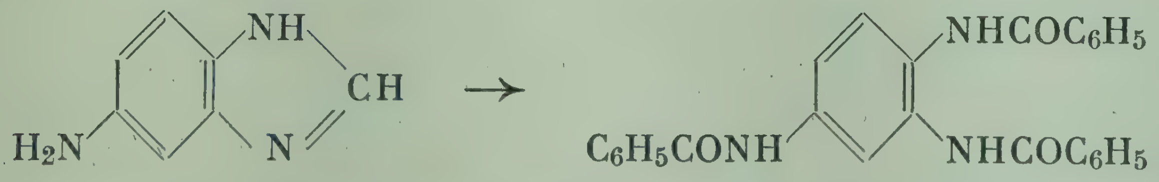
Sodium hydroxide *NaOH*

Ureas from amines and isocyanates $NH_2 \rightarrow NHCONHR$

s. *3*, 267; s. a. K. Zeile and M. Oetzel, Z. physiol. Chem. *284*, 1 (1949)

Imidazole ring opening C

355.

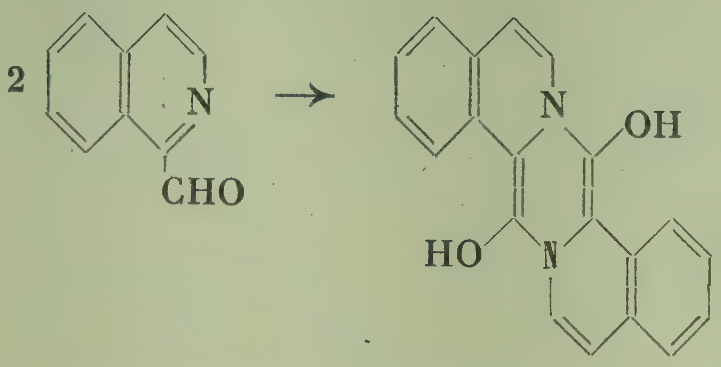


Benzoyl chloride added with vigorous stirring to a soln. of 12 gm. 5-aminobenzimidazole in 10%-NaOH, and heated 15 min. at 90-95° → 31 gm. 1,2,4-tribenzamidobenzene. F. e. s. M. Stäuble, Helv. *32*, 135 (1949).

Potassium cyanide *KCN*

Quinocolls ○

356.



A hot soln. of 1 gm. isoquinoline-1-aldehyde in aq. alcohol treated with aq. KCN, and refluxed 15 min. → 1 gm. crude dihydroisoquinocoll. F. e. s. B. R. Brown and D. L. Hammick, Soc. *1950*, 628.

Alkali salt ←

Ureas from amines $NH_2 \rightarrow NHCONH_2$

s. *4*, 460; s. a. F. Kurzer, Org. Synth. *31*, 8 (1951)

Pyridine *C_5H_5N*

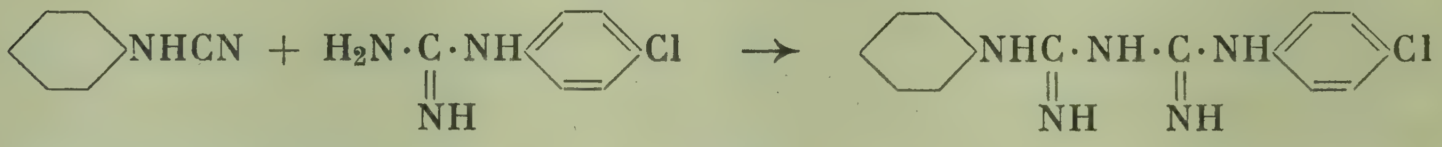
Ureas from amines and isocyanates $NH_2 \rightarrow NHCONHR$

s. *6*, 508

Magnesium *Mg*

Biguanides from cyanamides and guanidines ←

357.



Ethereal ethyl-MgI gradually added to a stirred suspension of p-chlorophenylguanidine in anisole, refluxed 15-30 min., cooled to room temp., a soln. of cyclohexylcyanamide in anisole added, refluxed 18-24 hrs. with stirring, ice-cooled, and decomposed with HCl-ice water → N^1-p-chlorophenyl-N^5-cyclohexyldiguanide (isolated as hydrochloride). Y: 69%. F. e. s. S. Birtwell, F. H. S. Curd, and F. L. Rose, Soc. *1949*, 2556.

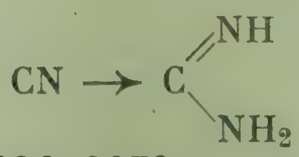
Acetic acid *CH_3COOH*

Sulfonylguanidines from sulfonylcyanamides ←

s. *6*, 529

Sulfonates *RSO_3^-*

Amidines from nitriles



$CN \rightarrow C(=NH)NH_2$

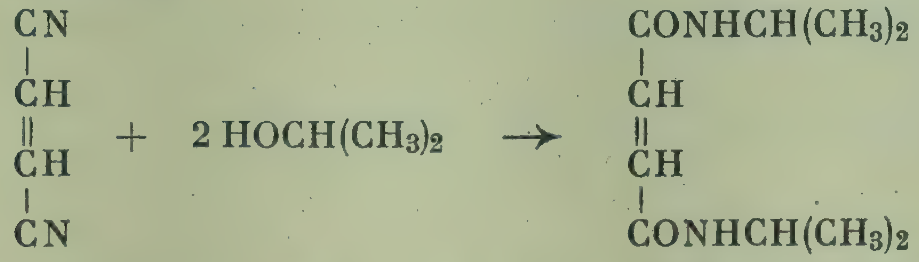
s. *2*, 326; s. a. L. Bauer and J. Cymerman, Soc. *1950*, 1826, 2078

Dihydroglyoxalines ○

s. *4,* 316; s. a. L. Bauer and J. Cymerman, Soc. *1950,* 2078

Sulfuric acid *H_2SO_4*

Subst. carboxylic acid amides from nitriles and alcohols CN → CONHR

358. 

$NC{-}CH{=}CH{-}CN + 2\,HOCH(CH_3)_2 \rightarrow (CH_3)_2CHNHCO{-}CH{=}CH{-}CONHCH(CH_3)_2$

Isopropanol added below 45° to a soln. of fumaronitrile in concd. H_2SO_4 over a period of 20 min., and worked up after 2 hrs. → N,N′-diisopropylfumaramide. Y: 80%. F. e. s. J. J. Ritter et al., Am. Soc. *71,* 4128, 4130 (1949); *72,* 5577 (1950).

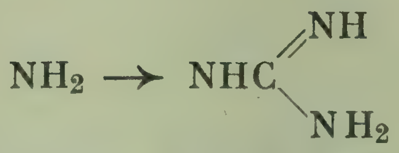
Hydrochlorides ←

Ureas from amines $NH_2 \rightarrow NHCONH_2$

359. $C_2H_5OOC \cdot CH_2NH_2 \rightarrow C_2H_5OOC \cdot CH_2NHCONH_2$

A warm aq. soln. of KCNO added in one portion to an aq. soln. of glycine ethyl ester hydrochloride, and warmed 15 min. on a steam bath → ethyl hydantoate. Y: 93%. W. E. Bachmann and C. E. Maxwell, 3rd., Am. Soc. *72,* 2880 (1950).

Guanidines from amines



s. *5,* 346; s. a. E. L. May, E. Mosettig, and H. G. Latham, Jr., J. Org. Chem. *15,* 890, 884 (1950)

Hydrochloric acid *HCl*

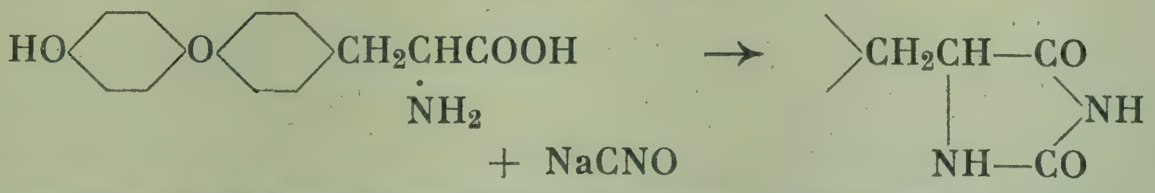
Thioureas from amines $NH_2 \rightarrow NHCSNH_2$

s. *1,* 363; s. a. F. Kurzer, Org. Synth. *31,* 21 (1951)

Carbamylmercaptoacetamides from amines $NH_2 \rightarrow NHCOCH_2SCONH_2$

s. *4,* 397; s. a. Am. Soc. *72,* 1687 (1950)

Hydantoins from α-aminocarboxylic acids ○

360. 

A suspension of 2 gm. thyronine in water containing Na-cyanate refluxed until all solid has dissolved, concd. HCl added, and refluxed for a further 30 min. → 1.9 gm. 5-(4-p-hydroxyphenoxybenzyl)hydantoin. F. e. s. J. C. Clayton and B. A. Hems, Soc. *1950,* 840.

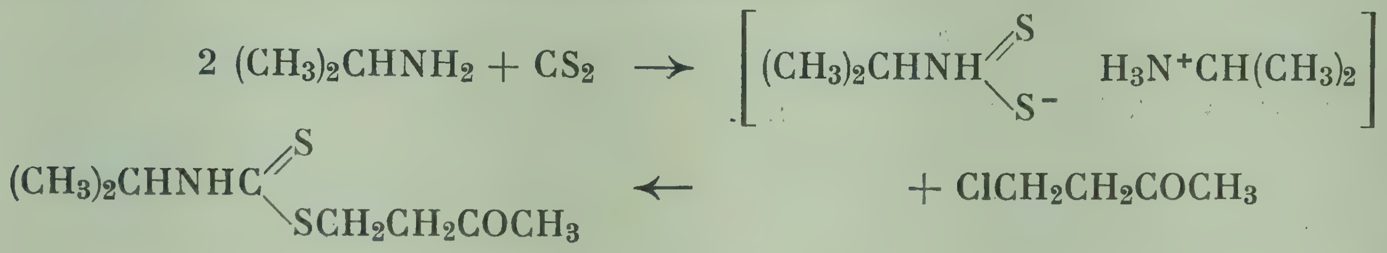
2-Mercaptoimidazoles from aminoacetals
s. *5*, 252; with KSCN s. Am. Soc. *71*, 4000 (1949)

Addition to Sulfur and Carbon NC ⇓ SC

Without additional reagents *w.a.r.*

Dithiocarbamic acid esters from amines ←

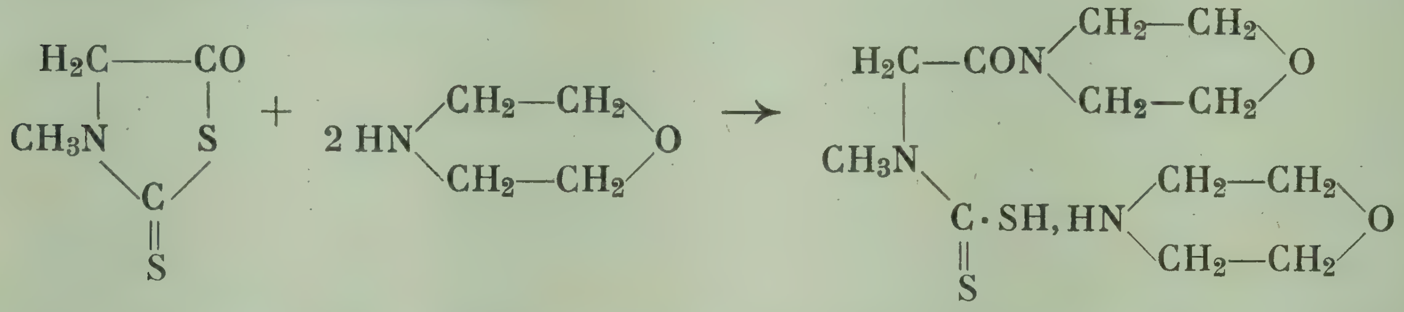
361.



CS_2 added to a well-stirred soln. of isopropylamine in alcohol, methyl 2-chloroethyl ketone added to the resulting suspension over a period of 0.5 hr., and allowed to stand at room temp. for 2 days → 3-ketobutyl isopropyldithiocarbamate. Y: 84%. J. W. Batty and B. C. L. Weedon, Soc. *1949*, 786.

Thiazolidine ring opening C

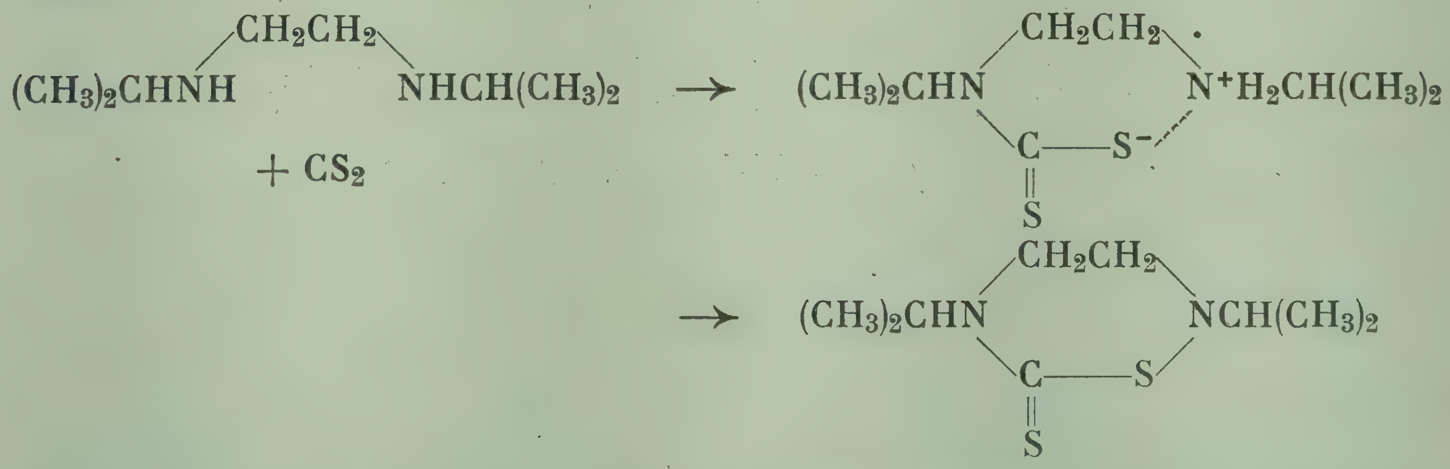
362.



2-Thio-3-methylthiazolid-5-one (prepn., s. 610) in acetone treated with 2 equivalents of morpholine → morpholinium salt of N-dithiocarboxy-N-methylaminoacetomorpholide. Y: 90%. A. H. Cook et al., Soc. *1949*, 2337; f. e. s. Soc. *1949*, 2323.

Tetrahydro-1,2,5-thiadiazine-6-thiones from diamines via amino-dithiocarbamic acids ○

363.



CS_2 in acetone added dropwise at 10-15° with vigorous stirring and cooling to a soln. of N,N′-diisopropylethylenediamine in acetone →

N-isopropyl-N-(β-isopropylaminoethyl)dithiocarbamic acid inner salt (Y: 90%) dissolved in 1.4 *N* aq. NaOH, then stirred vigorously, while aq. iodine KI-soln. is added dropwise, and worked up after precipitation is complete → 2,5-diisopropyltetrahydro-1,2,5-thiadiazine-6-thione (Y: 71%). F. e. s. R. A. Donia et al., J. Org. Chem. *14*, 946 (1949).

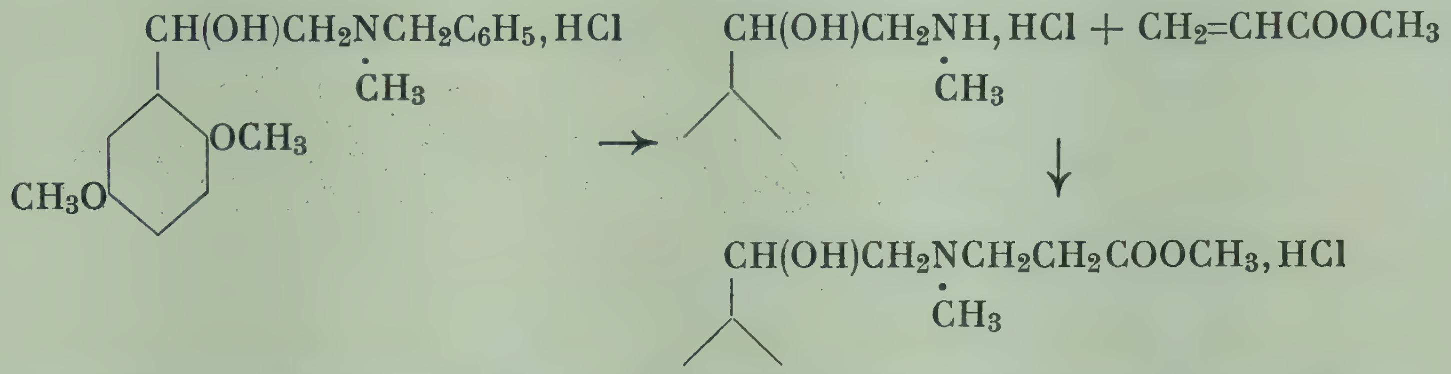
Addition to Carbon NC ⇓ CC

Without additional reagents *w.a.r.*

Amines from ethylene derivatives C:C → CHCN<

s. *2*, 328/9; *4*, 539; s. a. A. P. Phillips, Am. Soc. *72*, 3298 (1950)

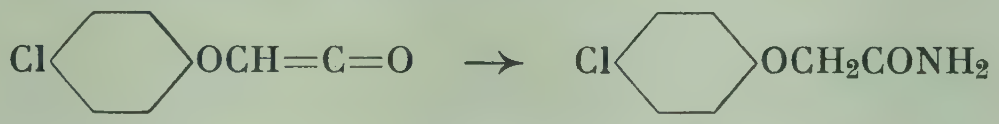
364.



Preceding **debenzylation.** A soln. of β-(2,5-dimethoxyphenyl)-β-hydroxyethyl-benzyl-methylamine hydrochloride in methanol hydrogenated with palladized charcoal → β-hydroxy-β-(2,5-dimethoxyphenyl)ethylmethylamine hydrochloride, the liberated base in benzene added to methyl acrylate, allowed to stand at room temp. for 3 days, warmed to ca. 50° for 3 hrs., and isolated as hydrochloride → N-methyl-N-(β-hydroxy-β-2,5-dimethoxyphenyl)ethyl-β-alanine methyl ester hydrochloride. Y: 90%. F. e. s. R. Baltzly and A. P. Phillips, Am. Soc. *71*, 3419, 3421 (1949).

Carboxylic acid amides from ketenes ←

365.



Dry NH_3-gas passed into an ethereal soln. of 4-chlorophenoxyketene (prepn. s. 883) until precipitation is complete → 4-chlorophenoxyacetamide. Y: 73%. F. e., also anilides, s. C. M. Hill, G. W. Senter, and M. E. Hill, Am. Soc. *72*, 2286 (1950).

Acetylation with ketene ←
Selective N-acetylation

366. $O(CH_2CH_2OH)_2 + 2\ O{=}C{=}CH_2 \rightarrow O(CH_2CH_2O\cdot COCH_3)_2$

Ketene introduced into diethyleneglycol in the presence of Na-acetate below 63° for 1.5 hrs. → diethyleneglycol diacetate. Y: 85%.—Only mixtures of mono-and diacetate are obtained in the absence of Na-acetate.

$HOCH_2CH_2NH_2 + O{=}C{=}CH_2 \rightarrow HOCH_2CH_2NHCOCH_3$

Ketene introduced into an aq. soln. of monoethanolamine → N-acetylaminoethanol. Y: 81.4%. Also diacetylation s. A. A. Ponomarev and Y. B. Isaev, Ж. *20*, 1079 (1950); C. A. *44*, 9349d.

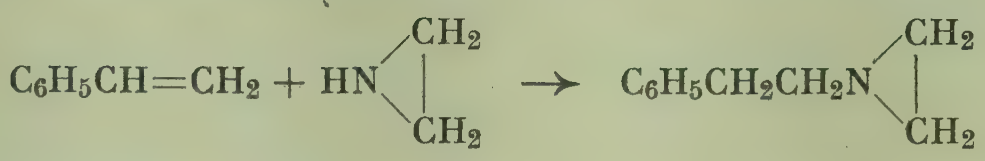
1,2,3-Triazoles from acetylene derivatives ○

s. *1*, 290; s. a. J. C. Sheehan and C. A. Robinson, Am. Soc. *73*, 1207 (1951)

Sodium *Na*

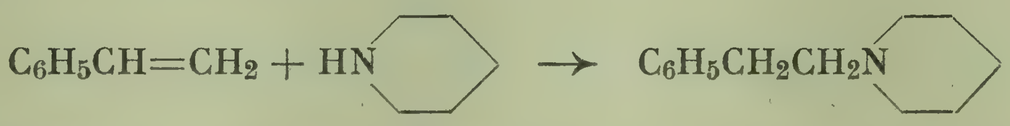
Amines from ethylene derivatives C:C → CHCN⟨

367.



Anhydrous ethyleneimine treated with Na, then with styrene at 25-45°, and stirring continued at room temp. for 5 hrs. → N-(β-phenylethyl)-ethyleneimine. Y: 89%. F. e. and reactions of ethyleneimine s. H. Bestian, A. *566*, 210 (1950).

368.

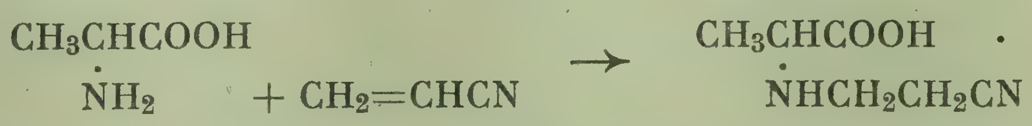


Phenylethylamines. 1-3% Na dissolved in refluxing piperidine, then styrene added dropwise over a period of 2 hrs., and refluxed for 3-5 hrs. more → N-(phenylethyl)piperidine. Y: 81%. F. e. with lower yields s. R. Wegler and G. Pieper, Chem. B. *83*, 1 (1950).

Bases

N-Cyanoethylation of α-aminocarboxylic acids C:C → CHCN⟨

369.



$$\underset{NH_2}{CH_3CHCOOH} + CH_2{=}CHCN \rightarrow \underset{NHCH_2CH_2CN}{CH_3CHCOOH}$$

By adding 1 equivalent of aq. NaOH, KOH, or $Ba(OH)_2$ followed by 1-1.1 equivalents of acrylonitrile below 30° to an aq. suspension of an α-amino acid, shaking until homogeneous, keeping overnight at 5° or room temp., and, if necessary, warming 2 hrs., at 50—60° to complete the reaction, N-monocyanoethyl-α-amino acids are obtained in good yields.—E: N-(2-Cyanoethyl)-DL-alanine. Y: 82.5%.—N-(2-Cyanoethyl)-L-leucine. Crude Y: 91%.—Racemization does not occur during the reaction. F. e. s. L. L. McKinney et al., Am. Soc. *72*, 2599 (1950); dicyanoethylation s. Am. Soc. *73*, 1641 (1951).

Borax *$Na_2B_4O_7$*

Carboxylic acid amides from α,α-dihalogenoethylene derivatives ←

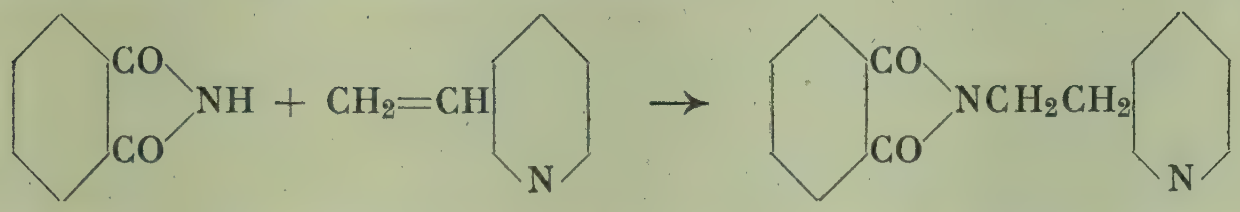
370. $$CF_2{=}CF_2 + H_2NC_6H_5 \rightarrow HCF_2CONHC_6H_5$$

A mixture of aniline, borax ($Na_2B_4O_7 \cdot 10\ H_2O$), and tetrafluoroethylene heated 8 hrs. with shaking at 130° → difluoroacetanilide. Y: 71%. F. e. s. D. D. Coffman et al., J. Org. Chem. *14,* 747 (1949).

Triton B ←

Phthalimides from ethylene derivatives $C:C \rightarrow CHCN<$

371.



Phthalimide, 2-vinylpyridine, and a little Triton B refluxed ca. 2 hrs. until the bath temp. reaches 188° without appreciable refluxing → N-[2-(2-pyridylethyl)]phthalimide. Y: 75%. F. K. Kirchner et al., J. Org. Chem. *14,* 388 (1949); method, see A. Galat, Am. Soc. *67,* 1414 (1945).

Salts of org. bases ←

N-Cyanoethylation
β-(Arylamino)propionitriles

372. $$C_6H_5NH_2 + CH_2{=}CHCN \rightarrow C_6H_5NHCH_2CH_2CN$$

Aniline, aniline acetate, and acrylonitrile heated in an oil bath at 120-140° for 14 hrs. → β-anilinopropionitrile. Y: 98%. F. e. s. A. F. Bekhli and A. G. Serebrennikov, Ж. *19,* 1553 (1949); C. A. *44,* 3448d.

Hydrazoic acid *HN_3*

Carboxylic acid amides from ketones ←

s. *4,* 326; s. a. D. V. Nightingale and R. M. Brooker, Am. Soc. *72,* 5539 (1950)

Sulfuric acid *H_2SO_4*

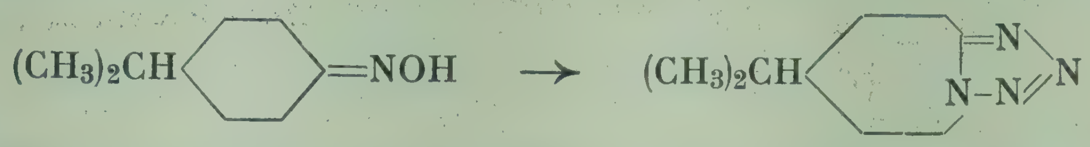
Subst. carboxylic acid amides from nitriles and ethylene derivatives ←

s. *5,* 258; s. a. Am. Soc. *71,* 4128, 4130 (1949); J. Heyboer and A. J. Staverman, R. *69,* 787 (1950)

Chlorosulfonic acid/sodium azide *$ClSO_3H/NaN_3$*

Tetrazoles from oximes ←
Ring enlargement

373.



Chlorosulfonic acid added below 35° to a vigorously stirred suspension of NaN_3 in ethylene dichloride, then 4-isopropylcyclohexane oxime in ethylene dichloride added dropwise at 35-45°, and stirring continued until the reaction mixture has cooled to room temp. → 8-isopropylpentamethylenetetrazole. Y: 67%. F. e. s. E. K. Harvill, C. W. Roberts, and R. M. Herbst, J. Org. Chem. *15*, 58, 671 (1950).

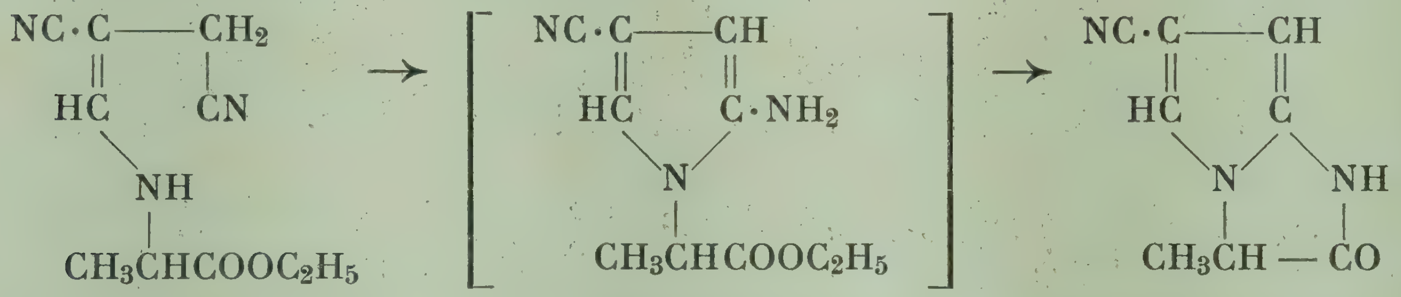
Rearrangement

Hydrogen/Nitrogen Type NC ↶ HN

Potassium/alcohol *KOR*

1,2-Dihydroimidazo[1,2-a]pyrroles via α-aminopyrroles from α-aminomethylene compounds ○

374.



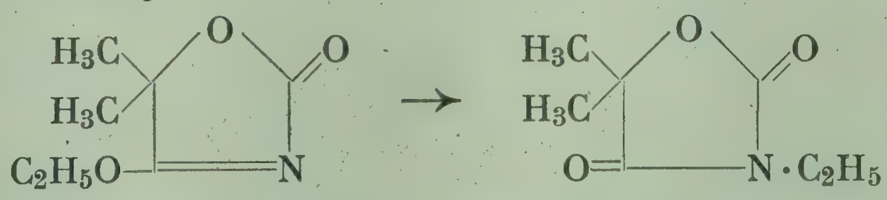
A soln. of α-[(1-carbethoxyethylamino)methylene]succinonitrile in abs. benzene added with stirring to a soln. of K in a mixture of abs. *tert*-amyl alcohol and benzene under N_2, and allowed to stand at room temp. for 3 hrs. → 2-oxo-3-methyl-6-cyano-1,2,3,4-tetrahydroimidazo[1,2-a]pyrrole. Y: 81%. F. e., also α-aminopyrroles, s. C. A. Grob and P. Ankli, Helv. *33*, 273 (1950).

Oxygen/Carbon Type NC ↶ OC

Without additional reagents *w.a.r.*

N-Alkyl from O-alkyl OR → NR

375.

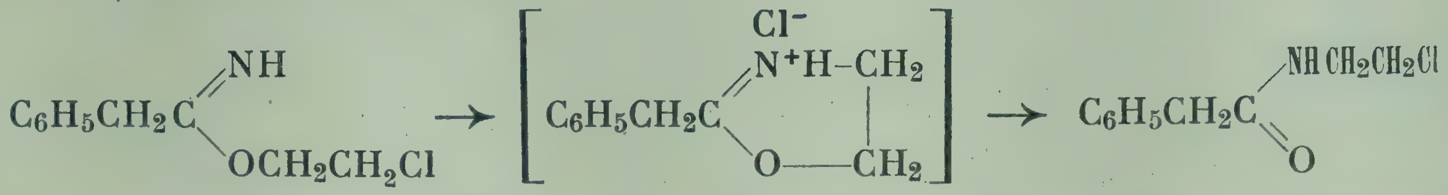


4-Ethoxy-5,5-dimethyloxazol-2-one heated at 180° for 24 hrs. → 5,5-dimethyl-3-ethyloxazolid-2,4-dione. Y: almost 100%. J. S. H. Davies and W. H. Hook, Soc. *1950*, 30; s. a. G. A. Wiese and J. W. Jones,

J. Am. Pharm. Assoc. *39*, 286 (1950); R. F. Rekker, H. Verleur, and W. T. Nauta, R. *70*, 5 (1951).

Subst. carboxylic acid amides from iminoesters via oxazolines ←

376.



Phenylacetimino 2-chloroethyl ether (from the hydrochloride) heated 1 hr. at 130° → N-2-chloroethylphenylacetamide. Y: 75%. F. e. s. M. W. Partridge and H. A. Turner, Soc. *1949*, 1308.

Bases ←

Acyl migration OAc → NAc

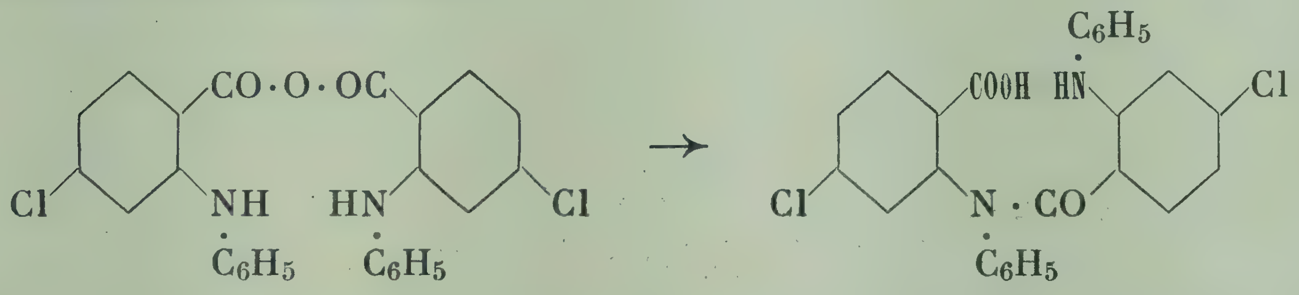
N-Acyl from O-acyl

s. *1*, 292; s. a. H. Bretschneider et al., M. *81*, 31 (1950)

Acetic acid *CH_3COOH*

Carboxylic acid amides from carboxylic acid anhydrides ←

377.



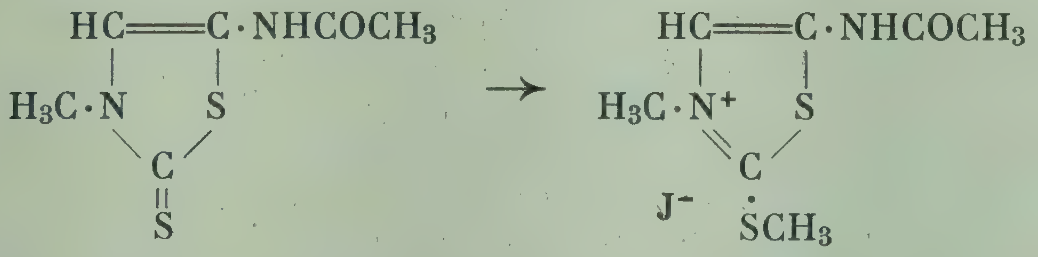
5-Chlorodiphenylamine-2-carboxylic acid anhydride in glacial acetic acid gently boiled for 1 hr. → (N-phenyl-p-chloroanthranoyl)-N-phenyl-p-chloroanthranilic acid. Y: 90%. F. e. s. A. M. Grigorovskiĭ, Ж. *19*, 1744 (1949); C. A. *44*, 2953c.

Sulfur/Carbon Type NC ∩ SC

Without additional reagents *w.a.r.*

Thiazolium salts from thiazolines ←

378.

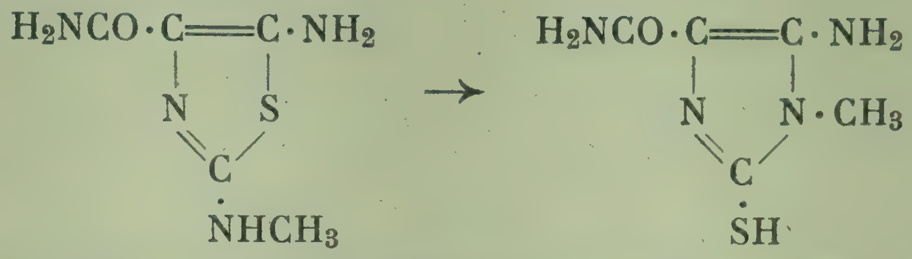


A suspension of 5-acetamido-2-thio-3-methylthiazoline (prepn. s. 610) in methanol refluxed 1 hr. with methyl iodide → 5-acetamido-2-methylmercapto-3-methylthiazolium iodide (startg. m. f. 178). Y: 80%. A. H. Cook and S. F. Cox, Soc. *1949*, 2337.

Sodium carbonate *Na_2CO_3*

Imidazoles from thiazoles ←

379.

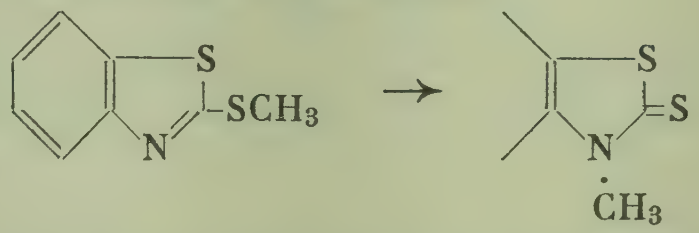


1.2 gm. 5-amino-2-methylaminothiazole-4-carboxamide refluxed 1 hr. with 1 *N* aq. Na-carbonate → 0.9 gm. 5-amino-2-mercapto-1-methylglyoxaline-4-carboxamide. A. H. Cook, I. Heilbron, and E. Smith, Soc. *1949*, 1440, 3001.

Iodine *I*

Thiazolethiones from mercapto thiazoles ←

380.



2-(Methylmercapto)benzothiazole heated with a little iodine at 210-220° for 4 hrs. in a sealed tube → 3-methyl-2 (3*H*)-benzothiazolethione. Y: 80%. A. I. Kiprianov and Z. N. Pazenko, Ж. *19*, 1523 (1949); C. A. *44*, 3487g.

Carbon/Carbon Type NC ∩ CC

Without additional reagents *w.a.r.*

Isocyanates from carboxylic acid azides $CON_3 \rightarrow C{:}C{:}O$

s. *6*, 470

Sodium nitrite *$NaNO_2$*

2-Oxazolidones from hydroxycarboxylic acid hydrazides ○

s. *5*, 263; s. a. E. D. Bergmann and M. Sulzbacher, J. Org. Chem. *16*, 84 (1951)

Sodium hypobromite *NaOBr*

Amines from carboxylic acid amides ←
via isocyanates
tert-Carbinamines
Hofmann degradation

381. $(n\text{-}C_4H_9)_3C\cdot CONH_2 \rightarrow (n\text{-}C_4H_9)_3C\cdot N{=}C{=}O \rightarrow (n\text{-}C_4H_9)_3C\cdot NH_2$

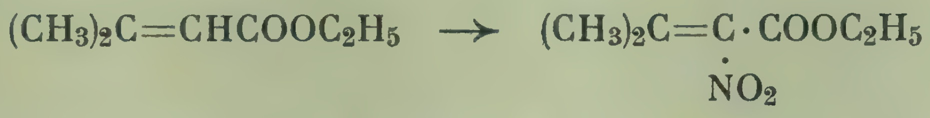
Br_2 added slowly with rapid stirring to ice-cold aq. NaOH, then finely powdered tributylacetamide added in one portion, and stirred vigorously for 4 hrs. at 0° → 1,1-dibutylamyl isocyanate (Y: 90%) heated 5 hrs. with 20%-HCl on a steam bath with stirring → 1,1-dibutylamylamine (Y: 72%). F. e. s. N. Sperber and R. Fricano, Am. Soc. *71*, 3352 (1949).

Exchange

Hydrogen ↑ NC⇅H

Without additional reagents *w.a.r.*

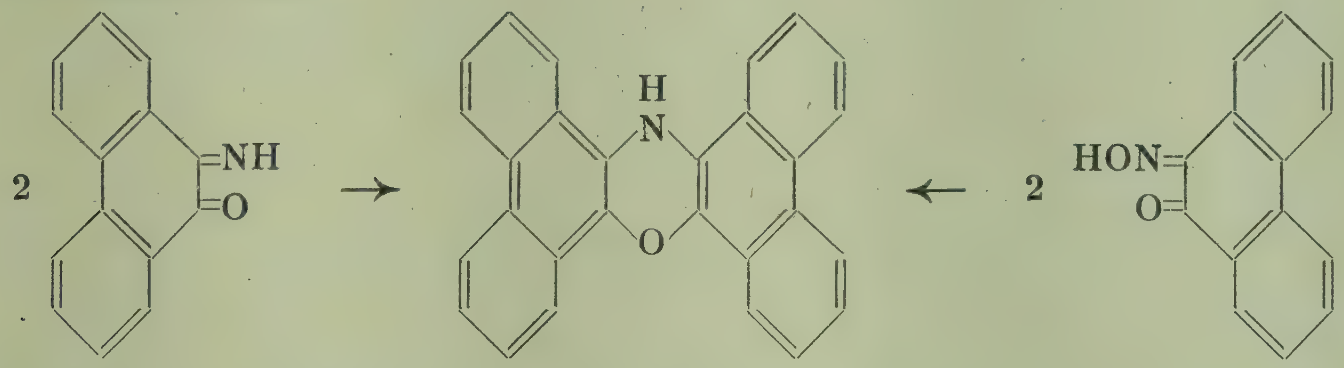
α-Nitro-α,β-ethylenecarboxylic acid esters from α,β-ethylenecarboxylic acid esters H → NO

382.


$$(CH_3)_2C{=}CHCOOC_2H_5 \rightarrow (CH_3)_2C{=}\underset{NO_2}{C}\cdot COOC_2H_5$$

Ethyl dimethylacrylate added with slow stirring below 5° to red HNO_3 (d. ca. 1.44) containing nitrogen oxides, and slow stirring continued at 20° for 5-6 hrs. → ethyl α-nitrodimethylacrylate (startg. m. f. 621). Y: 70-75%. R. Trave, G. *79*, 233 (1949); cf. O. Süs, W. Schäfer, and M. Grundkötter, A. *571*, 201 (1951).

Photoreduction ○
1,4-Oxazine ring

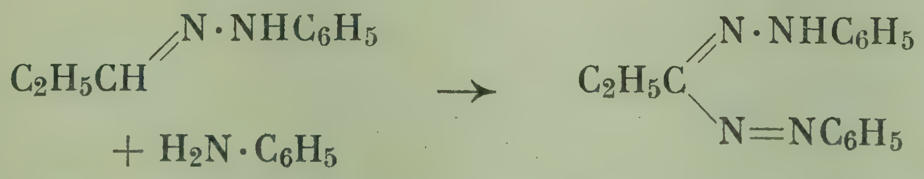
383.


Phenanthrenequinone-monoxime or -imine in isopropanol exposed to sunlight for 2 weeks → diphenanthroxazine. Y: ca. 100%. F. e. s. A. Schönberg et al., Soc. *1950*, 374.

Sodium acetate *CH_3COONa*

Aliphatic azo compounds by coupling N:N
s. *6*, 519

Formazans from hydrazones ←

384.


$$C_2H_5CH{=}N\cdot NHC_6H_5 + H_2N\cdot C_6H_5 \rightarrow C_2H_5C(=N\cdot NHC_6H_5)N{=}NC_6H_5$$

Aniline diazotized with aq. $NaNO_2$ in HCl, the diazonium salt soln. so obtained added at 0° to 3.2 gm. propionaldehyde phenylhydrazone and

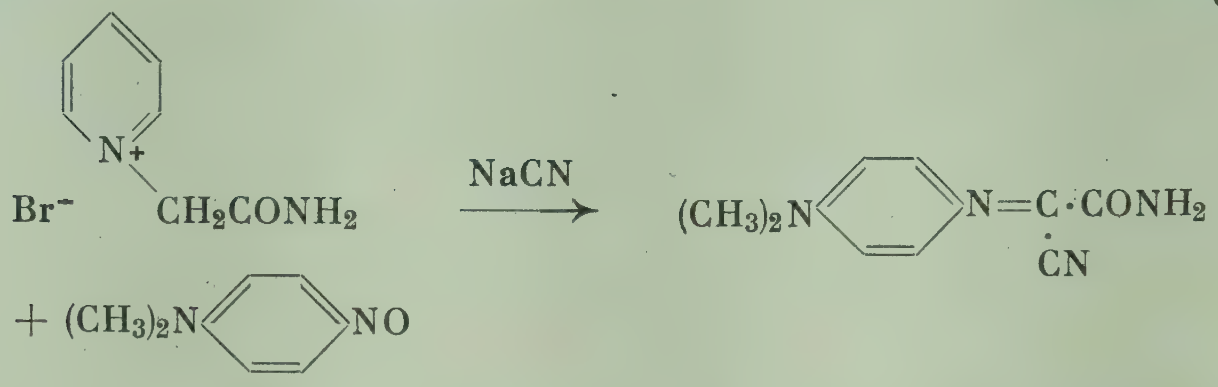
Na-acetate in methanol, and worked up after 14 hrs. → 3.5 gm. C-ethyl-N,N′-diphenylformazan. F. e. s. D. Jerchel et al., Chem. B. *82*, 515 (1949); A. *563*, 200, 208 (1949); with KOH s. S. W. Fox and E. Hemmingson Atkinson, Am. Soc. *72*, 3629 (1950).

Sodium cyanide *NaCN*

1,1-Cyanoimines from pyridinium salts

C=N·
ĊN

385.



An aq. soln. of NaCN added below 20° to (aminoformylmethyl)pyridinium bromide and nitrosodimethylaniline in alcohol → aminoformylglyoxylic acid nitrile p-dimethylaminoanil. Y: ca. 100%. F. e. s. F. Kröhnke, Chem. B. *83*, 50, 60 (1950).

Sodium nitrite *$NaNO_2$*

Nitrosation H → NO

s. *2*, 342; in dioxane s. R. F. Milligan and L. Koch, Am. Soc. *72*, 3811 (1950)

Nitration H → NO_2

s. *1*, 330; C. E. Clarkson, J. G. Holden, and T. Malkin, Soc. *1950*, 1556

Indazoles ○

s. *1*, 321; s. a. P. Petitcolas and R. Sureau, Bl. *1950*, 466

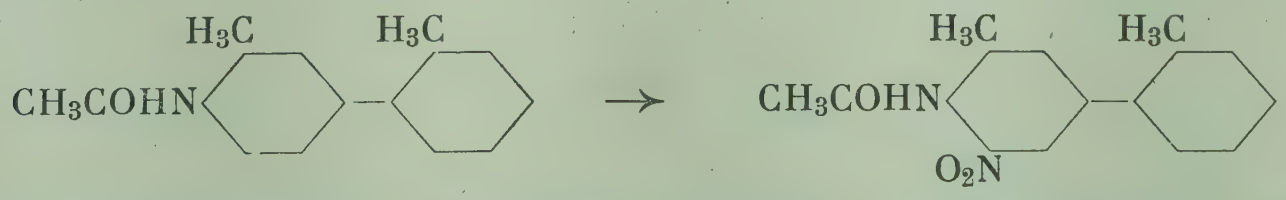
Alkali nitrate

Nitration H → NO_2

with KNO_3 s. *3*, 291; *4*, 337; with $NaNO_3$ s. H. Diaz de Arce, J. L. Greene, Jr., and J. D. Capps, Am. Soc. *72*, 2971 (1950)

Cupric nitrate *$Cu(NO_3)_2$*

386.



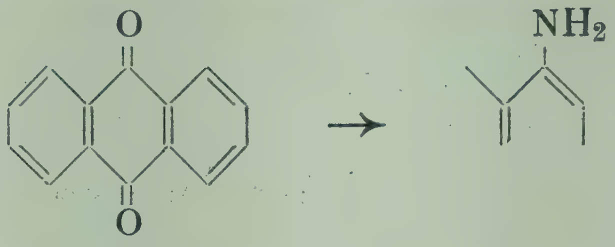
Powdered hydrated Cu(II)-nitrate added in small portions at 25-30° to a stirred, water-cooled suspension of 4-acetamido-3,2′-ditolyl in acetic anhydride, and worked up after 1 hr. → 5-nitro-4-acetamido-

3,2′-ditolyl. Y: 90%. M. C. Ford, W. A. Waters, and H. T. Young, Soc. *1950*, 833; isomers by different nitration procedures s. W. Davey and J. R. Gwilt, Soc. *1950*, 204; nitroaldehydes s. Soc. *1950*, 3348.

Vanadium pentoxide *V_2O_5*

Replacement of hydrogen by amino groups $H \rightarrow NH_2$

387.



Triacetylhydroxylamine (prepn. s. 227) added to a soln. of anthraquinone in concd. H_2SO_4 containing V_2O_5, and heated with stirring at 130-140° for 8 hrs. → 5.9 gm. 1-aminoanthraquinone (from 6.1 gm. anthraquinone converted). T. Urbanski, Soc. *1949*, 3374.

Molybdenum trioxide-alumina *MoO_3-Al_2O_3*

Nitriles from hydrocarbons $CH_3 \rightarrow CN$

388. $C_6H_5CH_3 \rightarrow C_6H_5CN$

Toluene and NH_3 passed over MoO_3 on activated Al_2O_3 at atmospheric pressure and 525-550° → benzonitrile. Y: 60-85%, based on toluene consumed; conversion 5-10% per pass. F. e. s. W. I. Denton et al., Ind. Eng. Chem. *42*, 796 (1950).

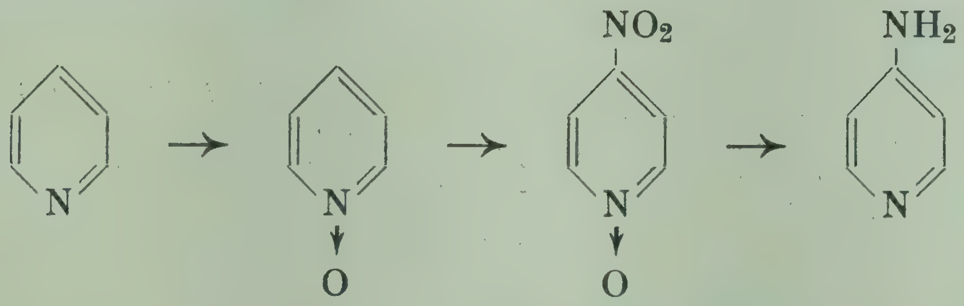
Sulfuric acid *H_2SO_4*

Nitration $H \rightarrow NO_2$

s. *6*, 593

Replacement of hydrogen by amino groups via nitro compounds
N-Oxides as intermediates

389.



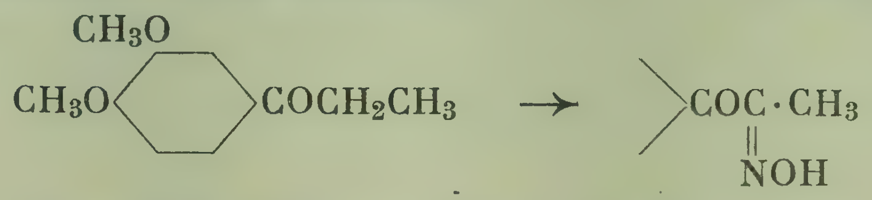
The N-oxide is used to make the pyridine nucleus accessible for substitution in positions 2 and 4.—E: Pyridine reacted with perphthalic acid in ether according to B. Bobranski, L. Kochanska, and A. Kowalewska, B. *71*, 2385 (1938) → pyridine-N-oxide phthalate (Y: ca. 100%) dissolved in H_2SO_4, added dropwise to a mixture of fuming HNO_3 and H_2SO_4, and heated 1.5 hrs. at 90° → 4-nitropyridine-N-oxide

(Y: 80-85%) heated 1 hr. at 100° with a mixture of Fe-powder and acetic acid → 4-aminopyridine (Y: ca. 100%). F. e. s. H. J. den Hertog and J. Overhoff, R. *69*, 468 (1950).

Hydrochloric acid *HCl*

α-Isonitrosoketones from ketones $COCH_2 \rightarrow COC{:}NOH$

390.



20%-HCl in abs. ether added to a soln. of ethyl 3,4-dimethoxyphenyl ketone in benzene, then isobutyl nitrite in abs. ether added portionwise with ice-cooling during 1 hr., and allowed to stand in ice overnight → isonitrosoethyl 3,4-dimethoxyphenyl ketone. Y: 95%. F. e. s. E. Karg, Arch. Pharm. *282*, 49 (1944); with dry HCl-gas and isoamyl nitrite s. J. A. Barltrop, A. J. Johnson, and C. D. Meakins, Soc. *1951*, 181.

Via intermediates *v.i.*

Aminophenols from phenols via azophenols $H \rightarrow NH_2$

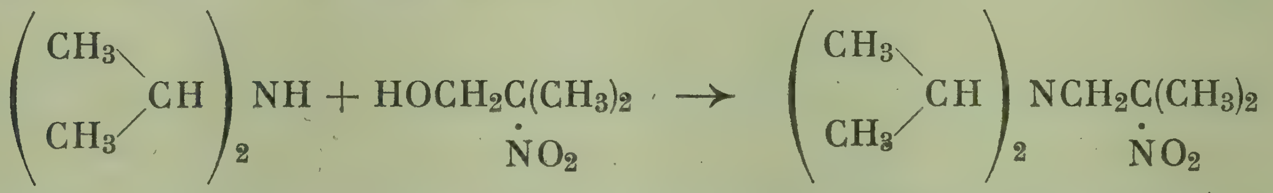
s. *5*, 267; s. a. D. Wasserman and C. R. Dawson, Am. Soc. *72*, 4994 (1950)

Oxygen ↑ NC ⇅ O

Without additional reagents *w.a.r.*

Nitramines from nitroalcohols OH → N<

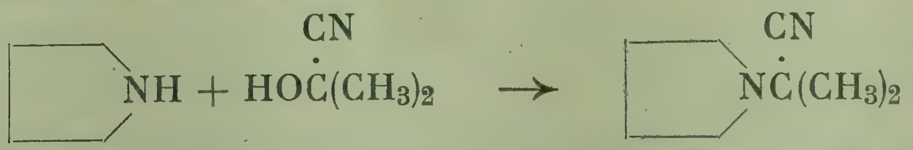
391.



A mixture of diisopropylamine and 2-nitro-2-methyl-1-propanol refluxed whereby the water formed is removed as an azeotrope with the excess diisopropylamine, and rectified after the formation of water has ceased → N-(2-nitroisobutyl)diisopropylamine. Conversion 87%. Reverse reaction s. 221. F. e. s. M. Senkus, Am. Soc. *72*, 2069 (1950).

α-Aminonitriles from cyanohydrins ←

392.

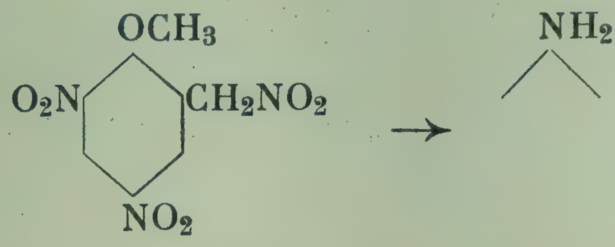


Pyrrolidine added slowly to acetone cyanohydrin, with slight cooling to keep the temp. below the boiling point → α-(1-pyrrolidyl)isobutyronitrile. Y: 88.7%. R. B. Moffett, J. Org. Chem. *14*, 862 (1949).

Prim. amines from ethers

OR → NH_2

393.

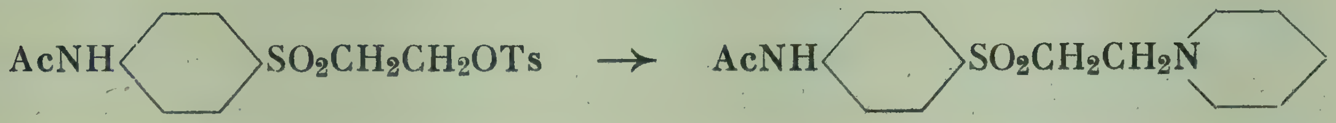


A soln. of 4,6-dinitro-2-nitromethylanisole in concd. aq. NH_3 kept at room temp. for 3 hrs. → 4,6-dinitro-2-nitromethylaniline. Y: 91%. G. Bendz et al., Soc. *1950*, 1130.

Amines from tosylates

OTs → N<

394.

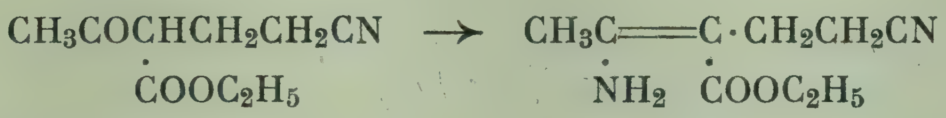


Piperidine added to 4-acetamidophenylβ-(p-toluenesulfonyloxy)ethyl sulfone, then heated on a steam bath for 2 hrs. → 4-acetamidophenyl β-piperidinoethyl sulfone. Y: 99%. F. e. s. B. R. Baker and M. V. Querry, J. Org. Chem. *15*, 413 (1950).

Prim. enamines from ketones

CHCO → C:C·NH_2

395.



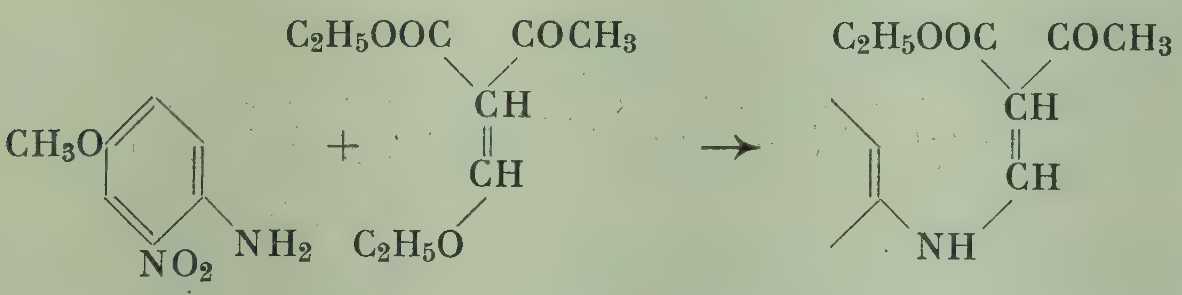
$$CH_3CO\underset{COOC_2H_5}{CH}CH_2CH_2CN \rightarrow CH_3\underset{NH_2}{C}{=}\underset{COOC_2H_5}{C}\cdot CH_2CH_2CN$$

NH_3-gas introduced into ethyl α-(β-cyanoethyl)acetoacetate at 80-90° for 6 hrs. → ethyl β-amino-α-(β-cyanoethyl)crotonate. Y: 77.5%. H. Henecka, Chem. B. *82*, 104 (1949); s. a. Ng. Ph. Buu-Hoï et al., J. Org. Chem. *14*, 802 (1949).

Enamines as intermediates in the quinoline ring synthesis

C:C·N<

396.



Equimolecular quantities of m-nitroanisidine and ethyl ethoxymethyleneacetoacetate heated 15 min. at 150° → ethyl α-acetyl-β-(o-nitro-p-methoxyanilino)acrylate. Y: ca. 100%.—Direct combination of the nitroanisidine, ethyl orthoformate, and acetoacetic ester is simpler but gives poorer yields. R. H. Baker et al., Am. Soc. *71*, 3060 (1949).

Enamines from α-hydroxymethylene compounds

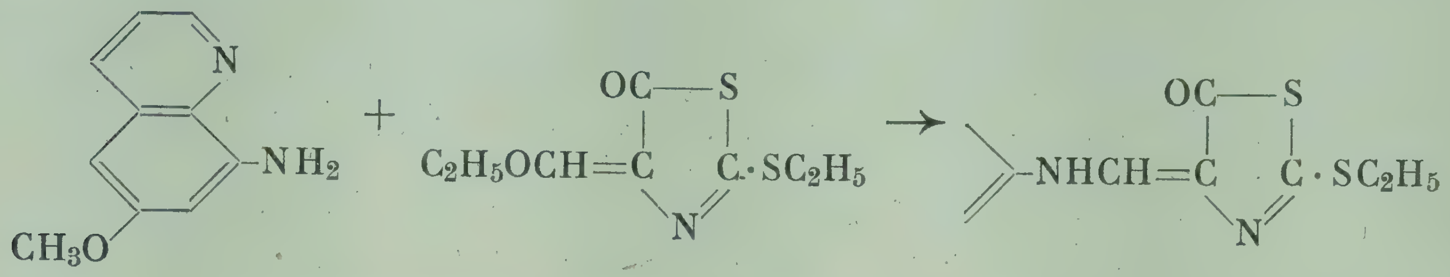
$\mathrm{C:C\cdot OH \rightarrow C:C\cdot N}<$

s. *2*, 725a; s. a. A. Cohen, Soc. *1950*, 3005

Enamines from α-alkoxymethylene compounds

$\mathrm{C:C\cdot OR \rightarrow C:C\cdot N}<$

397.



0.22 gm. 2-ethylmercapto-4-ethoxymethylene-5-thiazolone and 0.17 gm. 8-amino-6-methoxyquinoline mixed in ethanol → 0.35 gm. 2-ethylmercapto-4-(6′-methoxy-8′-quinolylaminomethylene)-5-thiazolone. A. H. Cook, G. Harris, and G. Shaw, Soc. *1949*, 1435.

s. a. *3*, 715; *5*, 269

Azomethines from amines and oxo compounds

$\mathrm{NH_2 \rightarrow N:C}$

s. *6*, 741

Reaction of nitroso compounds with active methylene groups

$\mathrm{NO \rightarrow N:C}$

s. *1*, 298; cf. Helv. *33*, 1648 (1950)

Reactions with isopropenyl acetate
Acetylamines

NHAc

s. *6*, 208

Carboxylic acid amides from carboxylic acids
Subst. carboxylic acid amides

$\mathrm{COOH \rightarrow CON}<$

s. *1*, 305; *5*, 276; s. a. G. Tsatsas, Bl. *1949*, 884

Carbalkoxycarboxylic acid amides from dicarboxylic acid esters

$\mathrm{COOR \rightarrow CON}<$

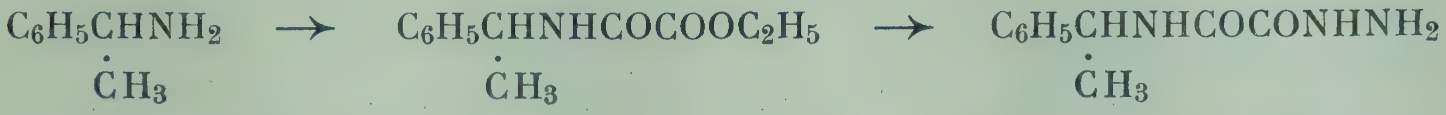
s. *6*, 844

Carboxylic acid imides from dicarboxylic acids

○

s. *2*, 363; s. a. R. B. Moffett, J. Org. Chem. *14*, 862 (1949)

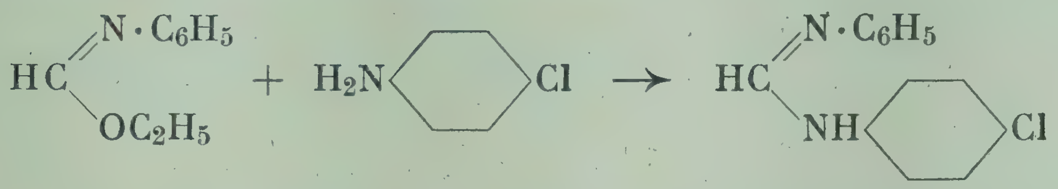
Carboxylic acid amide hydrazides from dicarboxylic acid esters via dicarboxylic acid amide esters ←

398. 

$$C_6H_5\underset{CH_3}{\dot{C}}HNH_2 \rightarrow C_6H_5\underset{CH_3}{\dot{C}}HNHCOCOOC_2H_5 \rightarrow C_6H_5\underset{CH_3}{\dot{C}}HNHCOCONHNH_2$$

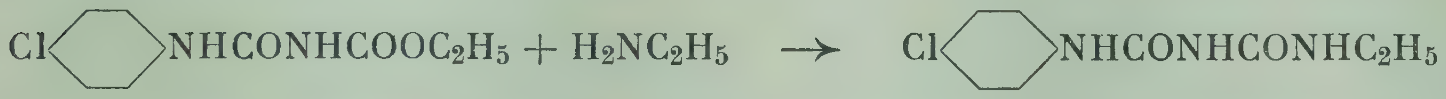
0.25 mole ethyl oxalate added slowly with stirring at room temp. to 0.12 mole α-phenylethylamine in abs. ethanol, and allowed to stand for 24 hrs. → ethyl N-(α-phenylethyl)oxamide (Y: 91%), dissolved in abs. ethanol, and 85%-hydrazine hydrate added with stirring → 5-(α-phenylethyl)semioxamazide (Y: 93%). N. J. Leonard and J. H. Boyer, J. Org. Chem. *15*, 42 (1950).

Formamidines from N-subst. iminoesters NHCH:NR

399. 

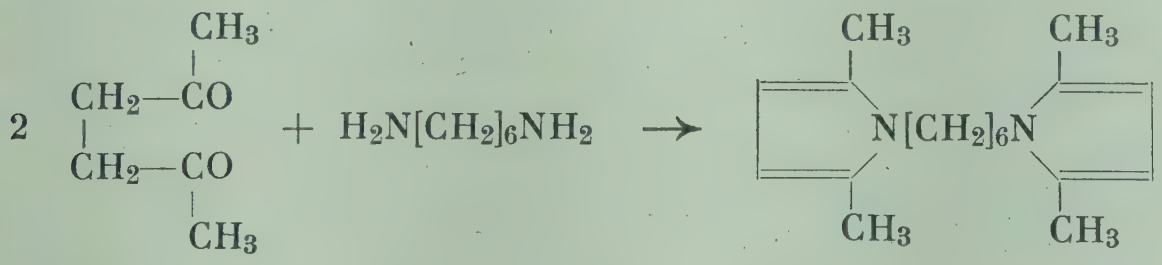
A mixture of p-chloroaniline and ethylisoformanilide heated 2 hrs. on a steam bath under slightly reduced pressure → N-phenyl-N′-p-chlorophenylformamidine. Y: ca. 100%. F. e. s. E. B. Knott and R. A. Jeffreys, J. Org. Chem. *14*, 879 (1949).

Biurets from carbalkoxyureas ←

400. 

5 gm. N-carbethoxy-N′-p-chlorophenylurea and 33%-aq.-ethylamine heated 1 hr. at 100° in a closed vessel → 4.1 gm. 1-(p-chlorophenyl)-5-ethylbiuret. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, Soc. *1949*, 1732.

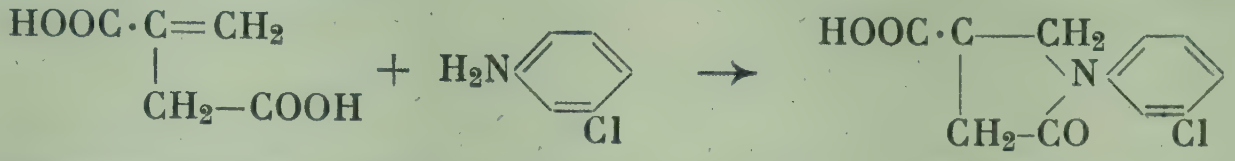
Pyrrole ring ○

401. 

A mixture of 1,6-diaminohexane and acetonylacetone refluxed 15 min. → 1,1-hexamethylenebis-(2,5-dimethylpyrrole). Y: almost 100%.—The reaction with ar. amines does not appear to be sensitive to steric hindrance when it is performed at high temp. without a solvent. F. e. s. Ng. Ph. Buu-Hoï, Soc. *1949*, 2882.

N-Subst. 2-pyrrolidones

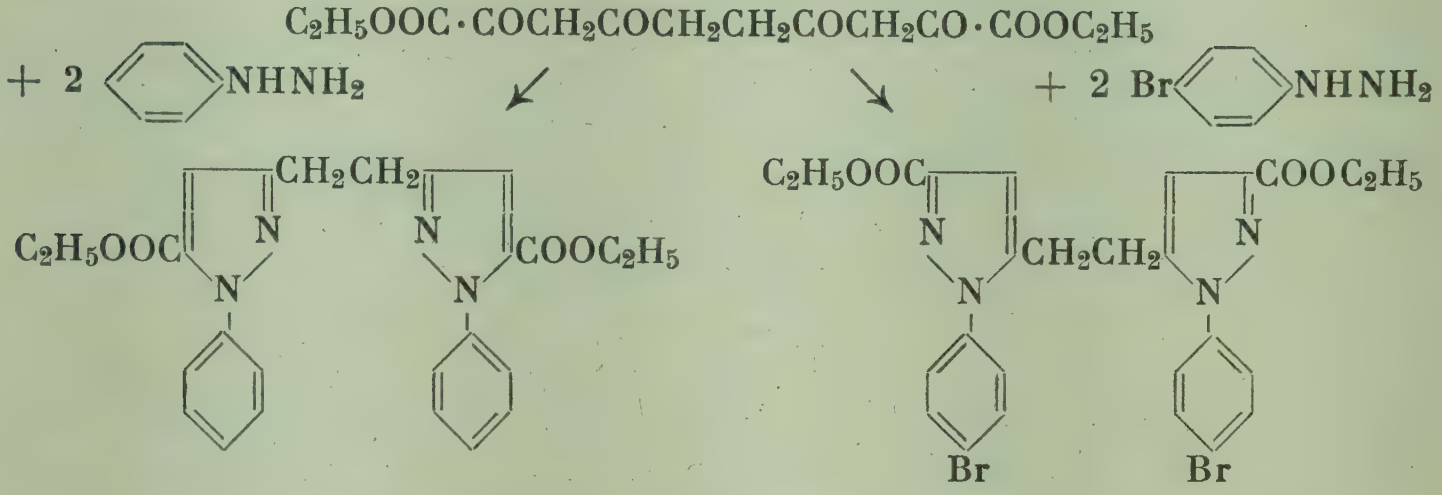
402.



m-Chloroaniline and itaconic acid maintained at the fusion point for 10-20 min. → 4-carboxy-1-(m-chlorophenyl)-2-pyrrolidone. Y: 84%. F. e. and limitations s. P. L. Paytash, E. Sparrow, and J. C. Gathe, Am. Soc. *72*, 1415 (1950); s. a. G. L. Evans, H. W. Gray, and H. W. Jacobson, Am. Soc. *72*, 2727 (1950).

Pyrazoles from β-diketones

403.



Diethyl α,γ,ξ,Θ-tetraketosebacate

(7.2 g.) reacted with phenylhydrazine in alcohol or glacial acetic acid → 5.5 g. 1,2-bis-(1-phenyl-5-carbethoxy-3-pyrazolyl)ethane.

(2.32 g.) reacted with p-bromophenylhydrazine in alcohol → 1.9 g. 1,2-bis-[1-(p-bromophenyl)-3-carbethoxy-5-pyrazolyl]ethane.

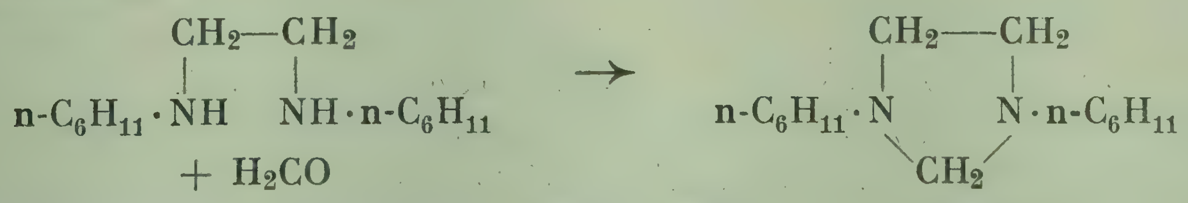
The reactivity of the carbonyl group depends on the arylhydrazine. With phenylhydrazine, the α-carbonyl group is the more reactive, whereas with p-bromophenyl and p-nitrophenyl-hydrazine the γ-carbonyl group is the more reactive. F. e. s. C. Musante and R. Beretti, G. *79*, 666 (1949).

Imidazole ring

s. *4*, 357; s. a. C. A. Salemink and G. M. van der Want, R. *68*, 1013 (1949); P. Mamalis, V. Petrow, and B. Sturgeon, Soc. *1950*, 1600

Imidazolidines

404.

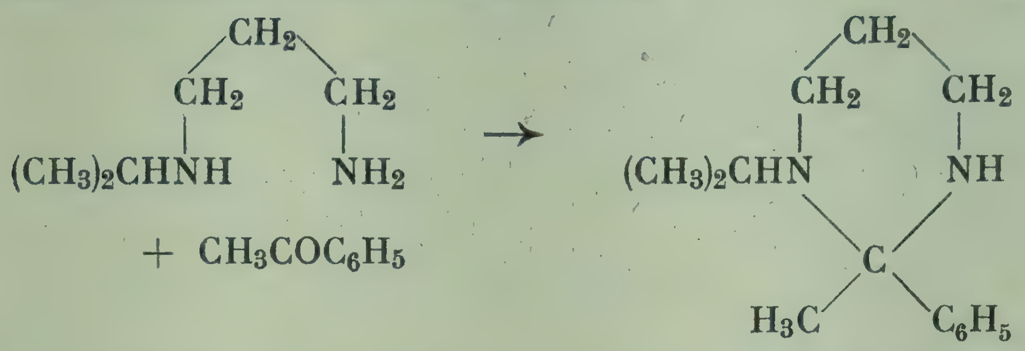


35—40%-formalin added below 50° to 10% excess of N,N-dicyclohexylethylenediamine → 1,3-dicyclohexylimidazolidine (startg. m. f. 616). Y: 79%. F. e. s. R. A. Donia et al., J. Org. Chem. *14*, 952 (1949); s. a.

J. L. Riebsomer, J. Org. Chem. *15*, 237 (1950); J. L. Boivin and G. F. Wright, Can. J. Research *28 B*, 213 (1950).

Hexahydropyrimidines from 1,3-diamines

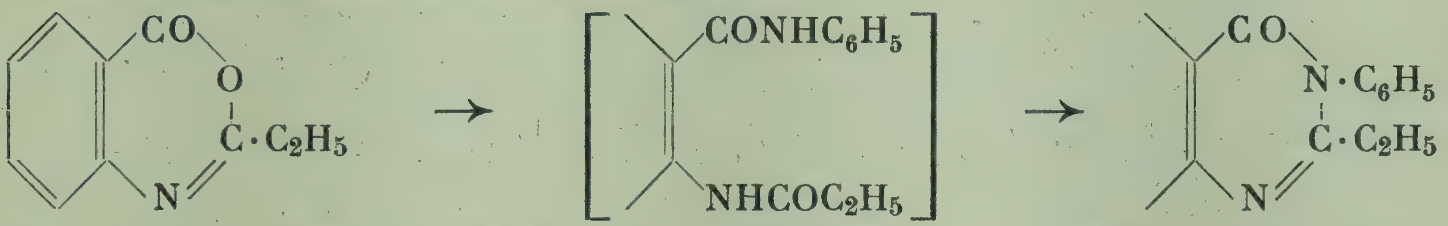
405.



N-Isopropyl-1,3-propanediamine, acetophenone, and a little benzene heated from 120° to 180° during a 6-hr.-period with distillation of the benzene-water azeotropic mixture → 1-isopropyl-2-methyl-2-phenylhexahydropyrimidine. Y: 57%. F. e. with higher yields s. J. L. Riebsomer and G. H. Morey, J. Org. Chem. *15*, 245 (1950).

Quinazolones from 3,1,4-benzoxazones

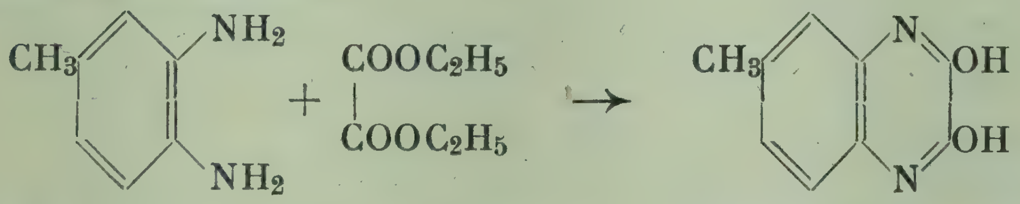
406.



A mixture of 2-ethyl-3,1,4-benzoxazone (prepn. s. 298) and aniline heated at 150—160° for 30 min. → 2-ethyl-3-phenyl-4-quinazolone. Y: 67.8%. F. e., also isolation of the intermediate, s. D. T. Zentmyer and E. C. Wagner, J. Org. Chem. *14*, 967 (1949).

2,3-Dihydroxyquinoxalines

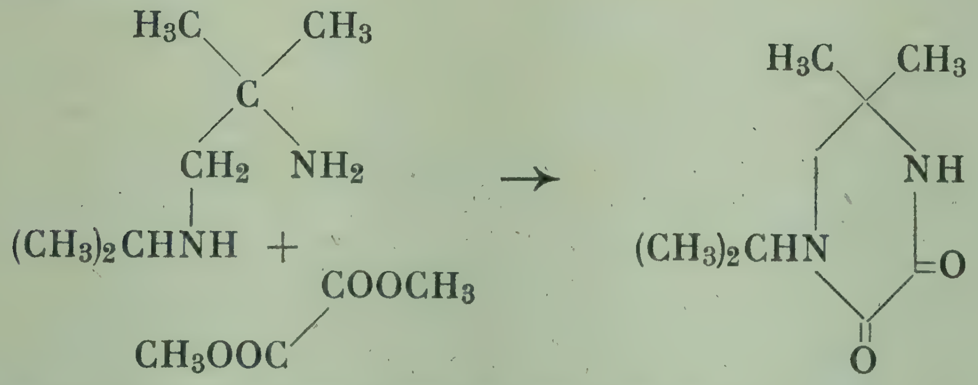
407.



Crude 4-methyl-1,2-phenylenediamine and ethyl oxalate heated at 170 to 180° for 3 hrs. → crude 2,3-dihydroxy-6-methylquinoxaline. Y: 94%. F. e. s. F. H. S. Curd, D. G. Davey, and G. J. Stacey, Soc. *1949*, 1271.

2,3-Piperazinediones

408.



A mixture of N-(2-aminoisobutyl)isopropylamine and dimethyl oxalate heated with distillation of the methanol formed, so that the temp.

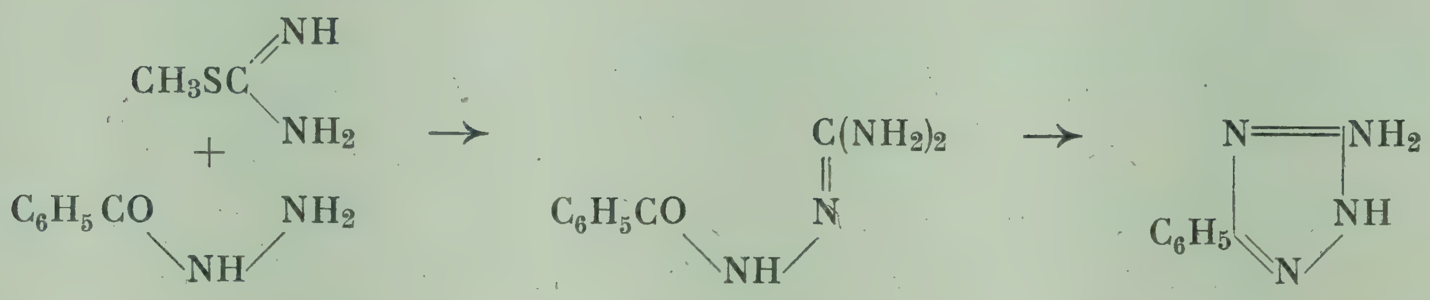
of the reaction flask is slowly increased during 4 hrs. to a maximum of 180° → 5,5-dimethyl-1-isopropyl-2,3-piperazinedione. Y: 63%. F. e. s. J. L. Riebsomer, J. Org. Chem. *15*, 68 (1950).

Photoreduction
1,4-Oxazine ring

s. *6*, 383

1,2,4-Triazoles from carboxylic acid hydrazides and isothioureas via acylaminoguanidines

409.

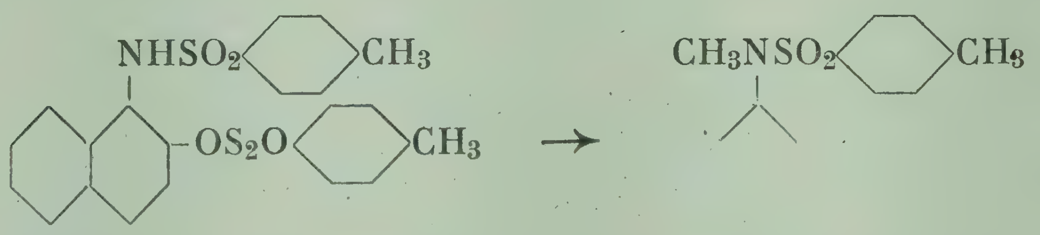


13.9 gm. S-methylisothiourea sulfate added with stirring to ice-cold *N* NaOH, followed by 13.5 gm. benzhydrazide, kept at room temp. 3-4 days, slowly warmed to 50°, and kept at this temp. for 3 hrs. → 12.2 gm. benzamidoguanidine, 5 gm. of which heated 5 min. just below its melting point at 220° → 3.8 gm. 5-amino-3-phenyl-1,2,4-triazole. F. e., also without isolation of the intermediate, s. E. Hoggarth, Soc. *1950*, 612.

Sodium hydroxide *NaOH*

N-Alkylation NH → NR

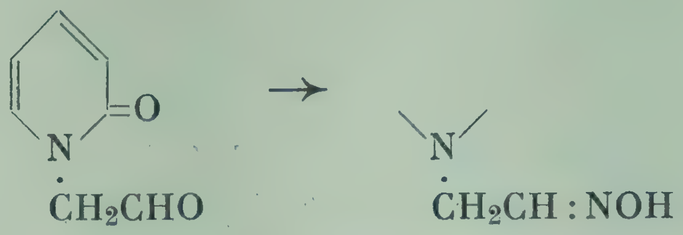
410.



A soln. of 1-p-toluenesulfonamido-2-naphthyl p-toluenesulfonate in acetone treated with vigorous stirring at 65-75° alternately with small portions of 30%-NaOH soln. and dimethyl sulfate over a period of 20 min., and refluxing continued for 0.5 hr. with addition of more NaOH soln. to keep the mixture alkaline → 1-p-toluenesulfonmethylamido-2-naphthyl p-toluenesulfonate (startg. m. f. 8). Y: almost 100%. F. Kurzer, Soc. *1949*, 3434.

Aldoximes CHO → CH:NOH

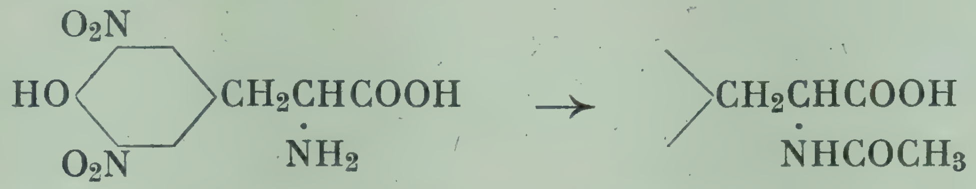
411.



A soln. of N-2-pyridone acetaldehyde hydrochloride and hydroxylamine hydrochloride in 95%-ethanol made just basic to litmus with 10%-aq.-NaOH, and evaporated to dryness on a steam-cone → N-2-pyridone acetaldoxime. Y: 85%. R. Adams and V. V. Jones, Am. Soc. *71,* 3826 (1949).

Acylamines from amines NH → NAc
Optically active compounds

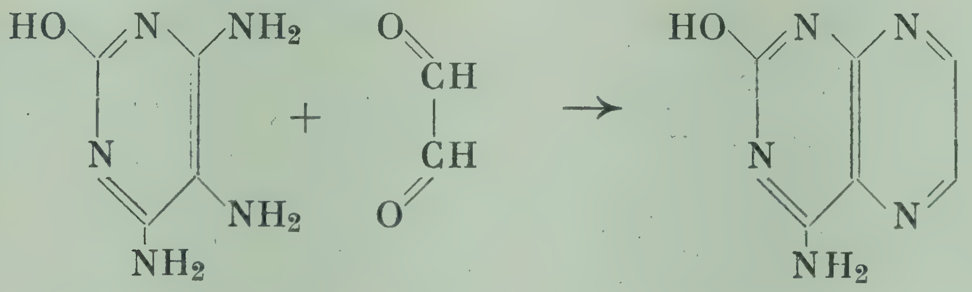
412.



A soln. of 3,5-dinitro-L-tyrosine in 2 *N* NaOH treated with stirring below 20° with acetic anhydride, stirring continued at room temp. for 1 hr., then warmed 30 min. at 40° in order to decompose excess acetic anhydride → 3,5-dinitro-N-acetyl-L-tyrosine. Y: 82%. J. R. Chalmers et al., Soc. *1949,* 3424; s. a. L. J. Reed, A. R. Kidwal, and V. du Vigneaud, J. Biol. Chem. *180,* 571 (1949).

Pyrimido[4,5-b]pyrazines ○

413.



Glyoxal bisulfite added to a soln. of 4,5,6-triamino-2-hydroxypyrimidine sulfate in water adjusted to pH 5 with dil. NaOH, heated to boiling, the pH adjusted to 9, and boiled 15 min. → 4-amino-2-hydroxypteridine. Y: 80%.—Because of the ready hydrolysis of the 4-amino group, it is necessary to effect the condensation in neutral or slightly alkaline soln. F. e. s. E. C. Taylor, Jr., and C. K. Cain, Am. Soc. *71,* 2538 (1949); cf. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, Soc. *1950,* 2743.

Potassium hydroxide *KOH*

α-Aminomethylene compounds from α-hydroxymethylene compounds C:CHN<

s. *6,* 511

Oximes

$C{:}O \rightarrow C{:}NOH$

s. *2*, 372; s. a. F. J. Villani and D. Papa, Am. Soc. *72*, 2722 (1950)

3,4-Dihydro-1,3,2H-benzoxazines

○

s. *5*, 288; cf. Am. Soc. *72*, 4691 (1950)

Sodium/alcohol *NaOR*

Alkoximes from isomeric oximes

$C{:}NOH \rightarrow C{:}NOR$

s. *6*, 462

Carboxylic acid amides from carboxylic acids

$COOH \rightarrow CONH_2$

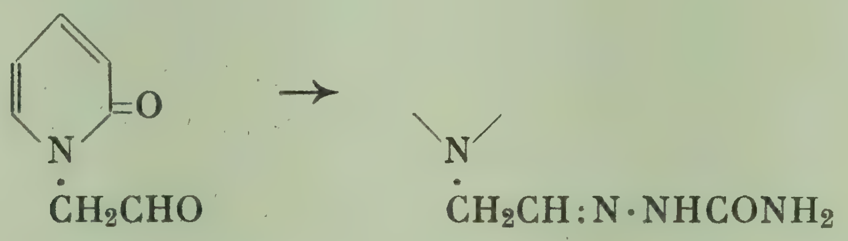
414. Ethyl ethylmalonate in a soln. of NH_3 and a little Na in methanol allowed to stand in a stoppered flask at room temp. for 96 hrs. → ethylmalondiamide. Y: 91%. F. e. s. P. B. Russell, Am. Soc. *72*, 1853 (1950).

Sodium acetate *CH_3COONa*

Semicarbazones

$C{:}O \rightarrow C{:}NNHCONH_2$

415.



An aq. soln. of N-2-pyridone acetaldehyde hydrochloride, semicarbazide hydrochloride, and Na-acetate heated 5 min. on a steam-cone → N-2-pyridone acetaldehyde semicarbazone. Y: ca. 100%. R. Adams and V. V. Jones, Am. Soc. *71*, 3826 (1949).

Ammonia *NH_3*

Dihydropyrazines from α-aminoketones

○

s. *4*, 367; with NH_3 s. G. Muller, G. Amiard, and J. Mathieu, Bl. *1949*, 533

Aniline *$C_6H_5NH_2$*

Osazones

←

416. The osazone-formation velocity of aldoses with phenylhydrazine in dil. acetic acid is considerably increased in the presence of aniline and can be used for the differentiation between aldoses and ketoses. F. Weygand and M. Reckhaus, Chem. B. *82*, 442 (1949).

Pyridine C_5H_5N

Diacylamines

$N(Ac)_2$

417. $C_2H_5OOC\cdot CH_2NHAc \rightarrow C_2H_5OOC\cdot CH_2N(Ac)_2$

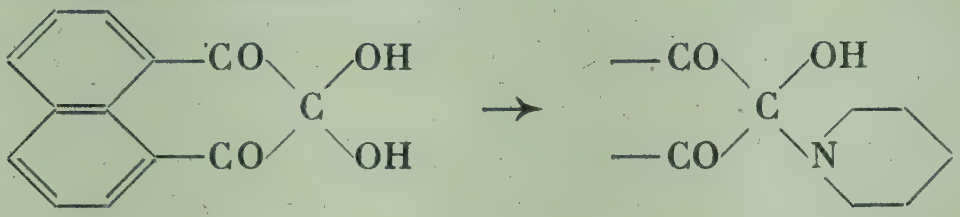
A mixture of acetylglycine ethyl ester, acetic anhydride, and pyridine gently refluxed with stirring for 6.5 hrs. → N,N-diacetylglycine ethyl ester. Y: 88%. F. e. s. R. H. Wiley and O. H. Borum, Am. Soc. *72*, 1626 (1950).

Piperidine $C_{5}H_{11}N$

1,1-Aminohydroxy compounds from 1,1-dihydroxy compounds

←

418.



1 gm. *peri*-naphthindane-1,2,3-trione hydrate in water and piperidine in alcohol mixed together, and worked up after 0.5 hr. → 1.2 gm. 2-hydroxy-2-(1′-piperidino)-*peri*-naphthindane-1,3-dione. F. e. s. R. Moubasher and W. I. Awad, Am. Soc. *1949*, 1137.

Calcium oxide CaO

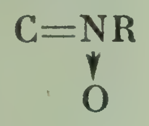
Hydrazones from ketones

C:O → C:NNH·

s. *6*, 450

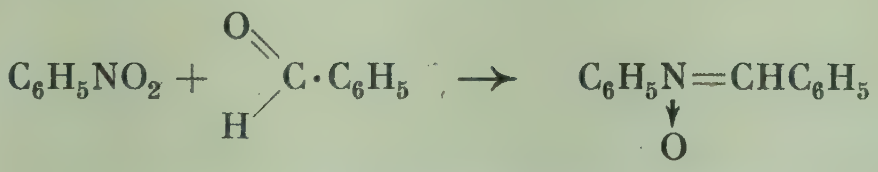
Zinc/acetic acid Zn/CH_3COOH

Nitrones from aldehydes and nitro compounds Isaldoximes



$\underset{\overset{\downarrow}{O}}{C=NR}$

419.



$$C_6H_5NO_2 + \overset{O}{\underset{H}{\diagdown}}C\cdot C_6H_5 \rightarrow C_6H_5\underset{\overset{\downarrow}{O}}{N}=CHC_6H_5$$

A mixture of nitrobenzene and benzaldehyde reacted with Zn-dust in alcohol-water-acetic acid at —8° over a period of 2 hrs. → phenylisobenzaldoxime. Y: 90%. F. e. s. J. Wiemann and C. Glacet, Bl. *1950*, 176.

Bauxite Al_2O_3

Sec. from prim. amines and alcohols Carboxylic acid esters and nitriles from carboxylic acids

←

420. Activated bauxite is an abundant and relatively inexpensive catalyst for drying and for dehydration reactions in organic chemistry. It has been found to be equal or superior to the various forms of activated

alumina. The yield obtained in dehydration reactions is affected by such variables as reaction temp., activation temp., and iron content of the bauxite.—E: Aniline and ethanol at 275° → ethylaniline. Y: 83.9%. —Capryl alcohol refluxed 2 hrs. with acetic acid → capryl acetate. Y: 82%.—Acetic acid and NH_3 at 425° → acetonitrile. Y: 95%. F. e. s. H. Heinemann, R. W. Wert, and W. S. W. McCarter, Ind. Eng. Chem. *41*, 2928 (1949).

Formamide $HCONH_2$

Amines from ketones $CO \rightarrow CHNH_2$
Leuckart reaction

s. *2*, 390; s. a. M. Métayer, P. Mastagli, and A. Bricard, Bl. *1950*, 1054

Papain ←

Enzymatic resolution of stereoisomers $COOH \rightarrow CONHR$
Carboxylic acid anilides
from carboxylic acids

s. *3*, 330; s. a. L. J. Reed, A. R. Kidwal, and V. du Vigneaud, J. Biol. Chem. *180*, 571 (1949); W. E. Hanby et al., Soc. *1950*, 3239

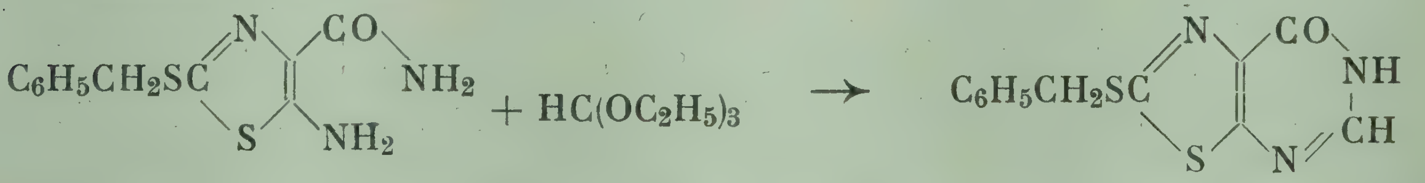
Acetic anhydride $(CH_3CO)_2O$

Formylation of amines $NH_2 \rightarrow NHCHO$

s. *2*, 391; s. a. H. R. Snyder and F. X. Werber, Am. Soc. *72*, 2962 (1950); with 90%-formic acid s. A. Stoll and E. Seebeck, Helv. *34*, 481 (1951)

Pyrimidine ring closure ○

421.



0.7 gm. 5-amino-2-benzylmercaptothiazole-4-carboxamide and ethyl orthoformate in acetic anhydride refluxed 2 hrs. → 0.8 gm. 6-keto-2′-benzylmercapto-1,6-dihydrothiazolo(5′,4′,4,5)pyrimidine. F. e. s. A. H. Cook and E. Smith, Soc. *1949*, 2329; pyrimido[4,5-b]pyrazines s. A. Albert, D. J. Brown, and G. Cheeseman, Soc. *1951*, 474.

Oxazole ring synthesis

s. *4*, 370; without Na-acetate s. C. Sannié and H. Lapin, Bl. *1950*, 322

Formic acid $HCOOH$

Leuckart-Wallach reaction $NH \rightarrow NR$

422. **Alkylation of amines with oxo compounds.** The alkylation is promoted by conditions which favor condensation. Formylation of the amine retards but does not prevent alkylation. E. and further results of a study of

this reaction s. E. Staple and E. C. Wagner, J. Org. Chem. *14,* 559 (1949). The advantage of using Na-formate in acetic acid lies probably in the diminished acidity of the medium and is apparent only when the starting amine is very feebly basic or has little tendency to add to the carbonyl group. The Leuckart-Wallach reaction is of some utility for the preparation of sec. amines when alkyl halides are unreactive (cyclohexyl halides) or react in undesired fashion (anisyl halides). E. s. R. Baltzly and O. Kauder, J. Org. Chem. *16,* 173 (1951); s. a. P. A. S. Smith and A. J. Macdonald, Am. Soc. *72,* 1037 (1950).

423.

$$(CH_3)_3C\cdot CH_2CH(CH_3)CH_2CHO + HN(CH_3)_2$$
$$\rightarrow (CH_3)_3C\cdot CH_2CH(CH_3)CH_2CH_2N(CH_3)_2$$

Amines from aldehydes. The alkylation of sec. amines with aliphatic aldehydes is initiated and completed at a generally lower temp. and under milder conditions than in other known instances of this reaction.—Procedure: The amine formate is first prepared by addition of the amine, as gas or liquid, to formic acid in 1 : 1 mole ratio. The temp. is then raised to ca. 60°, the aldehyde added dropwise over a 1-hr.-period, and the mixture generally heated on a steam bath for ca. 1 hr. until CO_2 evolution ceases.—E: 3,5,5-Trimethylhexaldehyde and dimethylamine → dimethyl-(3,5,5-trimethylhexyl)amine. Y: 84%. F. e. with lower yields and 2 step procedure (cf. 88) s. P. L. DeBenneville and J. H. Macartney, Am. Soc. *72,* 3073 (1950).

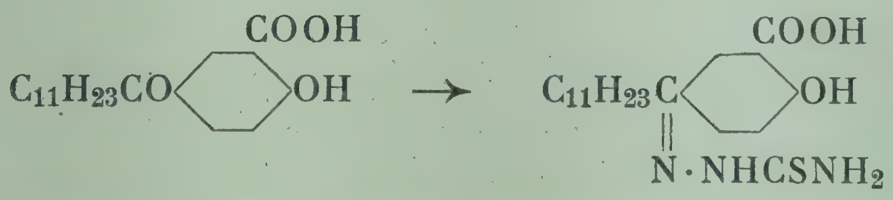
Acetic acid *CH_3COOH*

Azo compounds from quinones and hydrazines ←

s. *2,* 392; s. a. P. P. T. Sah, R. *69,* 1025 (1950)

Thiosemicarbazones $C{:}O \rightarrow C{:}N\cdot NHCSNH_2$

424.



Alc. thiosemicarbazide and some glacial acetic acid added to alc. 5-lauroylsalicylic acid, and refluxed 3.5 hrs. on a steam bath → 5-lauroylsalicylic acid thiosemicarbazone. Y: 98%. H. Bretschneider and H. Haas, M. *81,* 524 (1950).

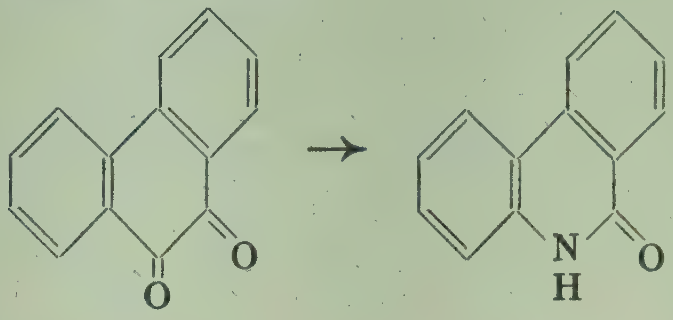
Phthalazines from o-ketocarboxylic acids ○

s. *3,* 335; s. a. Buu-Hoï, Hoán, and Xuong, R. *69,* 1083 (1950)

Sodium azide *NaN₃*

Phenanthridines from quinones ←

425.



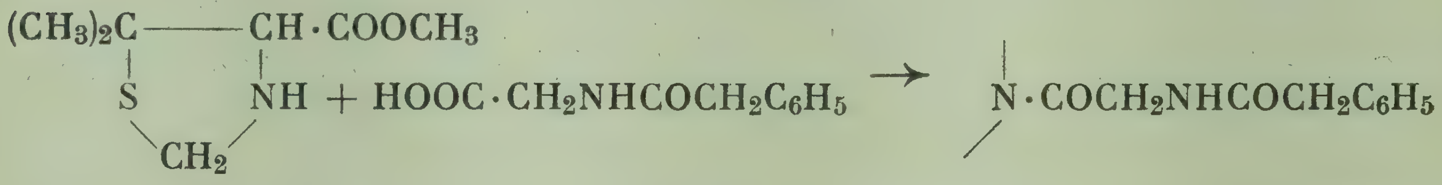
A soln. of 208 mg. phenanthrenequinone in concd. H_2SO_4 treated with finely powdered NaN_3 at 0-10°, then kept at room temp. for 2-3 hrs. until gas evolution has subsided and the original deep green color has faded → 180 mg. phenanthridone. E. F. M. Stephenson, Soc. *1949*, 2620.

Phosphorus trichloride *PCl₃*

Subst. carboxylic acid amides from carboxylic acids COOH → CONHR

Peptides

426.



$$\begin{array}{ccc} (CH_3)_2C & \text{——} & CH\cdot COOCH_3 \\ | & & | \\ S & & NH \\ & \diagdown CH_2 \diagup & \end{array} + HOOC\cdot CH_2NHCOCH_2C_6H_5 \rightarrow \begin{array}{c} | \\ N\cdot COCH_2NHCOCH_2C_6H_5 \\ \diagup \end{array}$$

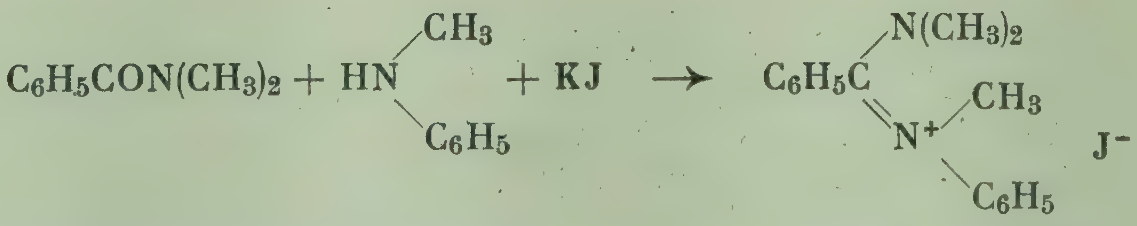
A mixture of 0.9 gm. methyl 5,5-dimethylthiazolidine-4-carboxylate, 1 gm. phenaceturic acid, and PCl_3 in abs. benzene refluxed 2 hrs. with stirring → 1.4 gm. methyl 3-phenaceturyl-5,5-dimethylthiazolidine-4-carboxylate. F. e. s. O. Süs, A. *564*, 54 (1949); peptides s. O. Süs and H. Hoffmann, A. *572*, 96 (1951).

s. a. *6*, 884

Phosphorus oxychloride *POCl₃*

Amidinium salts from carboxylic acid amides ←

427.

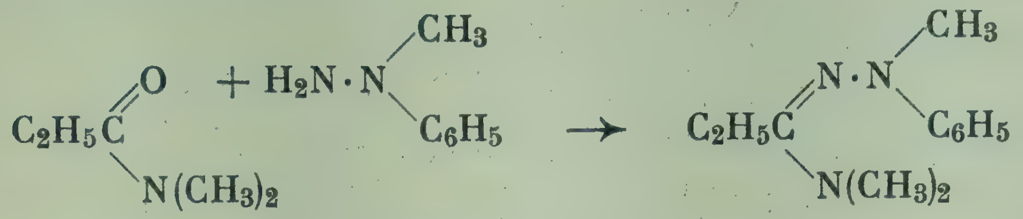


$$C_6H_5CON(CH_3)_2 + HN\begin{array}{l} \diagup CH_3 \\ \diagdown C_6H_5 \end{array} + KJ \rightarrow C_6H_5C\begin{array}{l} \diagup N(CH_3)_2 \\ \diagdown\!\!\diagdown N^+\begin{array}{l} \diagup CH_3 \\ \diagdown C_6H_5 \end{array} \end{array} J^-$$

Benzodimethylamide, methylaniline hydrochloride, and $POCl_3$ heated 5 hrs. at 120-130°, and worked up with addition of KI → N′-phenyl-N,N,N′-trimethylbenzamidinium iodide. Y: 90%. F. e. s. C. G. Raison, Soc. *1949*, 3319.

Amidrazones from carboxylic acid amides and hydrazines ←

428.

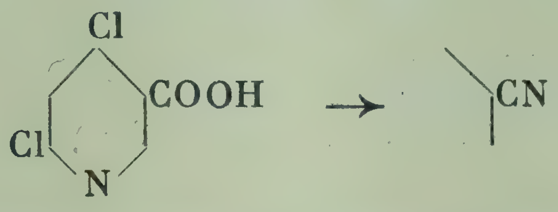


A soln. of α-methyl-α-phenylhydrazine and N,N-dimethylpropionamide in dry benzene added to a stirred, refluxing soln. of $POCl_3$ in benzene, stirring and refluxing continued for 5 hrs. → N^1,N^3,N^3-trimethyl-N^1-phenylpropionamidrazone. Y: 82%. F. e. s. H. Rapoport and R. M. Bonner, Am. Soc. *72*, 2783 (1950).

Phosphorus oxychloride/phosphorus pentachloride *$POCl_3/PCl_5$*

Nitriles from carboxylic acids COOH → CN

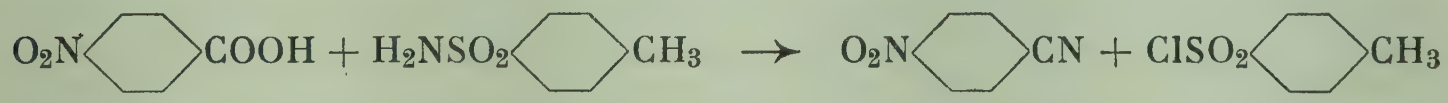
429.



A mixture of 2,4-dichloropyridine-5-carboxylic acid and $POCl_3$ heated to 100°, PCl_5 gradually added, heated 0.5 hr. at 140°, $POCl_3$ distilled off in vacuo, the residue dissolved in benzene, and NH_3-gas passed into the soln. → 2,4-dichloropyridine-5-carbonitrile (startg. m. f. 532). Y: 95%. H. J. den Hertog et al., R. *69*, 673 (1950).

Phosphorus pentachloride/p-toluenesulfonic acid amide *$PCl_5/TsNH_2$*

430.



PCl_5 added with stirring to a mixture of p-nitrobenzoic acid and p-toluenesulfonamide, warmed gently in a hot-air bath to initiate the reaction, after subsiding of the first reaction gradually heated to ca. 205°, and maintained at this temp. until no more material distils → p-nitrobenzonitrile. Y: 85-90%.—Aliphatic acids give low yields and, in some cases, chlorinated by-products. F. e. s. C. S. Miller, Org. Synth. *29*, 75 (1949).

Sulfamide/pyridine *$SO_2(NH_2)_2/C_5H_5N$*

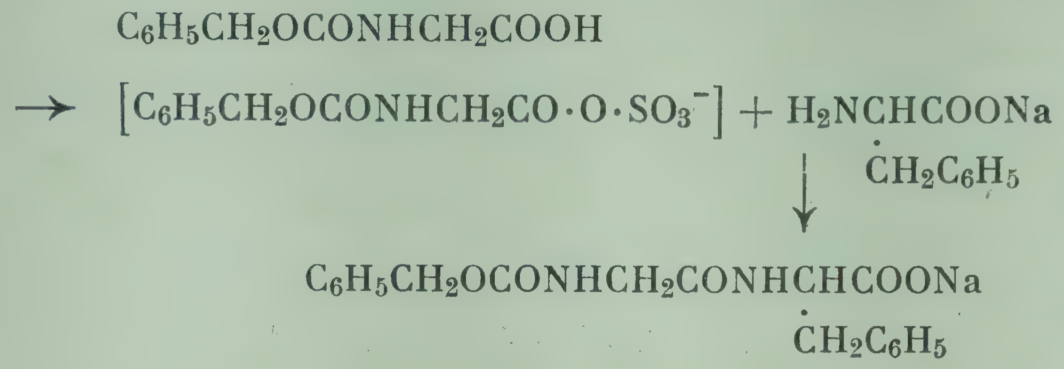
Carboxylic acid amides from carboxylic acids COOH → $CONH_2$

431. Benzoic acid, sulfamide, and pyridine heated on a steam bath for 3 hrs. → benzamide. Y: 84.3%. F. e. s. A. V. Kirsanov and Y. M. Zolotov, Ж. *19*, 2201 (1949); C. A. *44*, 4446g; cf. *20*, 1637 (1950); C. A. *45*, 1950c

Dimethylformamide-sulfur trioxide complex $HCON(CH_3)_2,SO_3$

Peptides COOH → CONHR

432.



$$C_6H_5CH_2OCONHCH_2COOH$$
$$\rightarrow [C_6H_5CH_2OCONHCH_2CO\cdot O\cdot SO_3^-] + H_2N\underset{CH_2C_6H_5}{CH}COONa$$
$$\downarrow$$
$$C_6H_5CH_2OCONHCH_2CONH\underset{CH_2C_6H_5}{CH}COONa$$

A soln. of carbobenzoxyglycine in dimethylformamide neutralized with methanolic phenyltrimethylammonium methoxide, a portion of the solvent distilled off at 50° in vacuo whereby methanol and traces of water are removed, the homogeneous soln. of the phenyltrimethylammonium salt of carbobenzoxyglycine cooled to 0°, an equivalent of SO_3 in dimethylformamide added, followed after 1 min. by an aq. soln. of Na-L-phenylalanine and sufficient NaOH to restore the pH to 9 → carbobenzoxyglycyl-L-phenylalanine. Y: 72%. F. e. s. G. W. Kenner, Chemistry and Industry *1951,* 15.

Sulfuric acid H_2SO_4

Monosubst. ureas from alcohols OH → $NHCONH_2$

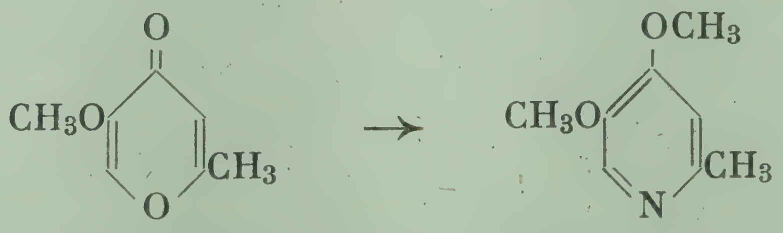
433. $(CH_3)_3C\cdot OH + H_2NCONH_2 \rightarrow (CH_3)_3C\cdot NHCONH_2$

Finely powdered urea added slowly at 20-25° to concd. H_2SO_4, then *tert*-butyl alcohol added dropwise at the same temp., stirred for an additional 0.5 hr., and allowed to stand at room temp. for ca. 16 hrs. → *tert*-butylurea (startg. m. f. 494). Y: 31-33%. F. e. s. L. I. Smith and O. H. Emerson, Org. Synth. *29,* 18 (1949).

Perchloric acid $HClO_4$

Pyridine ring from pyrone ring ←
Baeyer reaction

434.

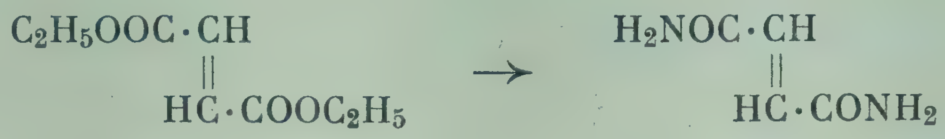


A mixture of 30 gm. 2-methyl-5-methoxy-4-pyrone and dimethyl sulfate heated 2 hrs. at 50°, cooled in an ice bath, added to a twofold excess of cold 20%-$HClO_4$, allowed to stand for 2 hrs., filtered, the crystalline methoperchlorate added in portions to cold 10% NH_4-carbonate soln., and allowed to come to room temp. → 20 gm. crude 2-methyl-4,5-dimethoxypyridine. K. N. Campbell, J. F. Ackerman, and B. K. Campbell, J. Org. Chem. *15,* 221 (1950).

Ammonium chloride *NH_4Cl*

Carboxylic acid amides from carboxylic acid esters $COOR \rightarrow CONH_2$

435.



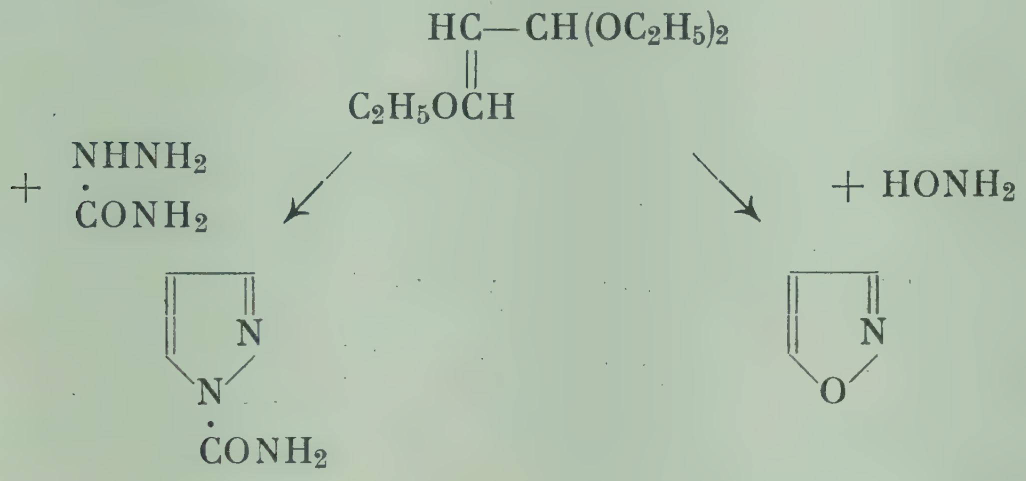
$$\begin{array}{l}C_2H_5OOC\cdot CH\\ \quad\| \\ HC\cdot COOC_2H_5\end{array} \rightarrow \begin{array}{l}H_2NOC\cdot CH\\ \quad\| \\ HC\cdot CONH_2\end{array}$$

A mixture of diethyl fumarate, concd. aq. NH_3, and NH_4Cl stirred 7 hrs. at 25-30° with slight cooling → fumaramide. Y: 80-88%. D. T. Mowry and J. M. Butler, Org. Synth. *30*, 46 (1950).

Hydrochlorides ←

Pyrazoles and isoxazoles from enolether acetals ○

436.



β-Ethoxyacrolein diethylacetal

shaken with aq. semicarbazide hydrochloride for 15 min. → pyrazole-1-carboxylic acid amide. Y: 87%.

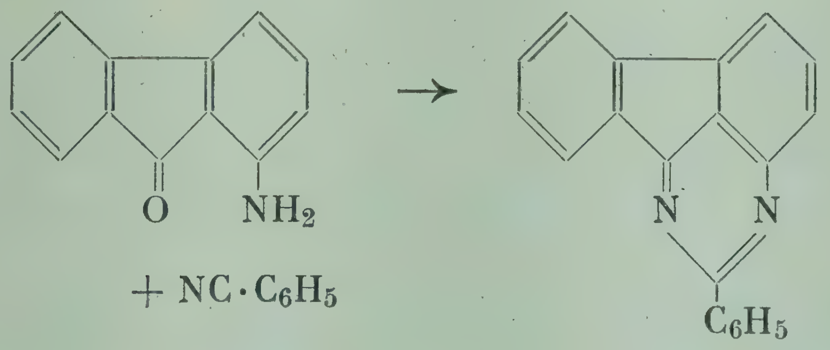
refluxed 1 hr. with aq. hydroxylamine hydrochloride in a water bath → isoxazole. Y: 67%.

F. e. s. A. Dornow and K. Peterlein, Chem. B. *82*, 257 (1949); pyridine ring with β-ethoxyacrolein diethylacetal s. 735.

Hydrochloric acid *HCl*

2,4-Diazafluoranthenes

437.



Dry HCl passed at 180-185° into a mixture of 1 gm. 1-aminofluorenone and 5 c.c. benzonitrile during 11 hrs. → 0.9 gm. 3-phenyl-2,4-diazafluoranthene. F. e. s. J. W. Cook and J. S. Moffatt, Soc. *1950*, 1160.

Nickel *Ni*

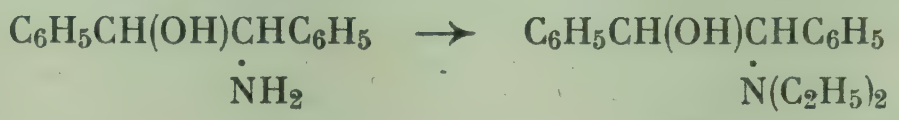
Amines from oxo compounds ←

s. *3*, 350; *4*, 401; *5*, 313; also from unsatd. oxo compounds s. P. Mastagli, M. Metayer, and A. Bricard, Bl. *1950*, 1045

Palladium-barium sulfate/aluminum chloride *Pd-BaSO$_4$/AlCl$_3$*

Tert. from prim. and sec. amines NH → NR

438.



$$C_6H_5CH(OH)\underset{NH_2}{CH}C_6H_5 \rightarrow C_6H_5CH(OH)\underset{N(C_2H_5)_2}{CH}C_6H_5$$

By hydrogenation of a mixture of certain amines and an oxo compound with Pd-BaSO$_4$ in the presence of an activator, e.g. AlCl$_3$, ZnCl$_2$, HCl, tert. amines can be obtained from prim. and sec. amines. In the absence of an activator, sec. amines are obtained only. E: A soln. of 10.5 gm. *iso*-α-hydroxy-β-amino-α,β-diphenylethane in methanol treated with acetaldehyde and AlCl$_3$·6H$_2$O, and hydrogenated with Pd-BaSO$_4$ at room temp. and 3.4 atm. until the theoretical amount of H$_2$ has been absorbed → 6.5 gm. *iso*-α-hydroxy-β-diethylamino-α,β-diphenylethane. F. e. s. W. Stühmer and W. Neumann, Chem. B. *83*, 66 (1950).

Platinum oxide *PtO$_2$*

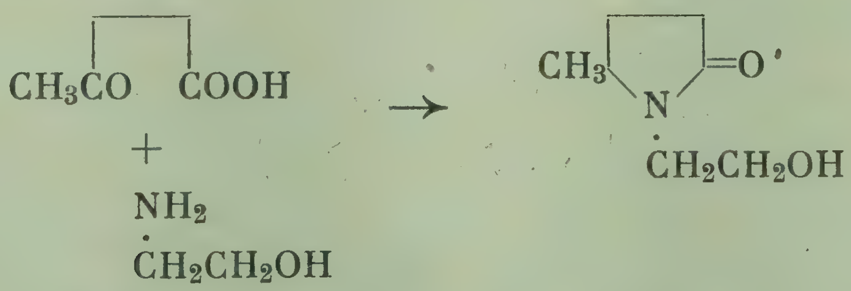
Sec. from prim. amines and oxo compounds

Aminoalcohols

439. cf. 4, 406. When the aminoalcohol contains a catechol nucleus, only ketones can be employed. A nuclear amino group may be alkylated simultaneously if an excess of carbonyl compound is used. F. s. E. L. Engelhardt, F. S. Crossley, and J. M. Sprague, Am. Soc. *72*, 2718 (1950).

2-Pyrrolidones from γ-ketocarboxylic acids ○

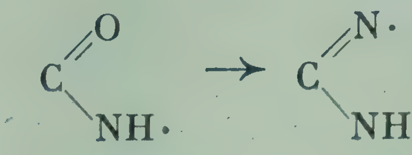
440.



A suspension of PtO$_2$ in abs. ethanol hydrogenated to Pt, a soln. of levulinic acid and ethanolamine in abs. alcohol added, and hydrogenated ca. 4 hrs. at 50 lbs./sq.in. and room temp. until the theoretical quantity of H$_2$ is absorbed → 1-(2-hydroxyethyl)-5-methyl-2-pyrrolidone. Y: 95%. F. e. s. R. B. Moffett, J. Org. Chem. *14*, 862 (1949).

Via intermediates *v.i.*

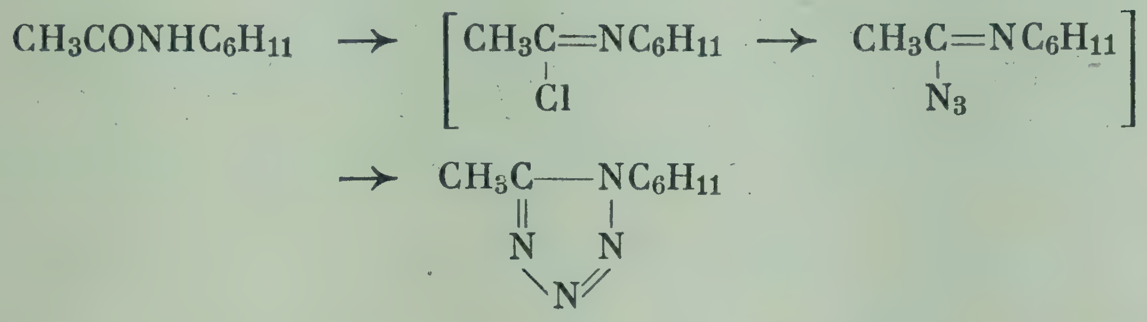
Amidines from subst. carboxylic acid amides



s. *1*, 351; s. a. A. C. Hontz and E. C. Wagner, Org. Synth. *31*, 48 (1951)

Tetrazoles from carboxylic acid amides via iminochlorides

441.



$CH_3CONHC_6H_{11} \rightarrow \left[\underset{Cl}{CH_3C}{=}NC_6H_{11} \rightarrow \underset{N_3}{CH_3C}{=}NC_6H_{11} \right]$

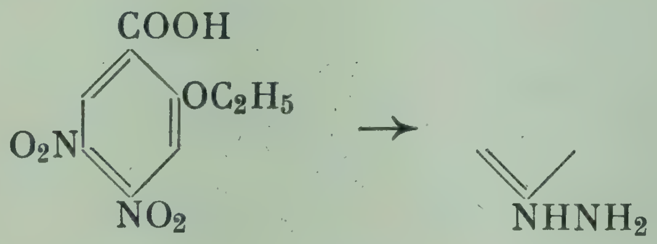
PCl_5 added portionwise to a stirred and cooled soln. of N-cyclohexylacetamide in benzene, HN_3 in benzene added after PCl_5 has disappeared, the mixture allowed to stand 1 hr. at room temp. after the vigorous reaction has subsided, then gradually warmed to the boiling point on a water bath, and maintained at this temp. ca. 3 hrs. until the HCl evolution has ceased → 1-cyclohexyl-5-methyltetrazole. Y: 51%. F. e. s. E. K. Harvill et al., J. Org. Chem. *15*, 662 (1950).

Nitrogen ↑ NC ⇅ N

Without additional reagents *w.a.r.*

Replacement of mobile nitro groups by hydrazino groups $NO_2 \rightarrow NHNH_2$

442.

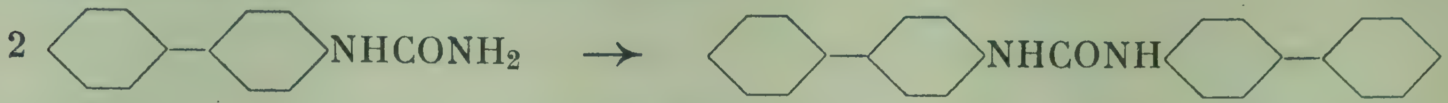


A soln. of 4,5-dinitro-2-ethoxybenzoic acid and hydrazine hydrate in alcohol heated 0.5 hr. on a steam bath → 5-nitro-4-hydrazino-2-ethoxybenzoic acid (startg. m. f. 509). Y: 85%.—Similarly with phenylhydrazine: 5-nitro-4-phenylhydrazino-2-ethoxybenzoic acid. Y: 78%. H. Goldstein and R. Brochon, Helv. *32*, 2334 (1949); f. e. s. Helv. *34*, 146 (1951).

Ureas from amines $NH_2 \rightarrow NHCONH_2$

s. *4*, 413; s. a. W. E. Bachmann et al., Am. Soc. *72*, 3132 (1950)

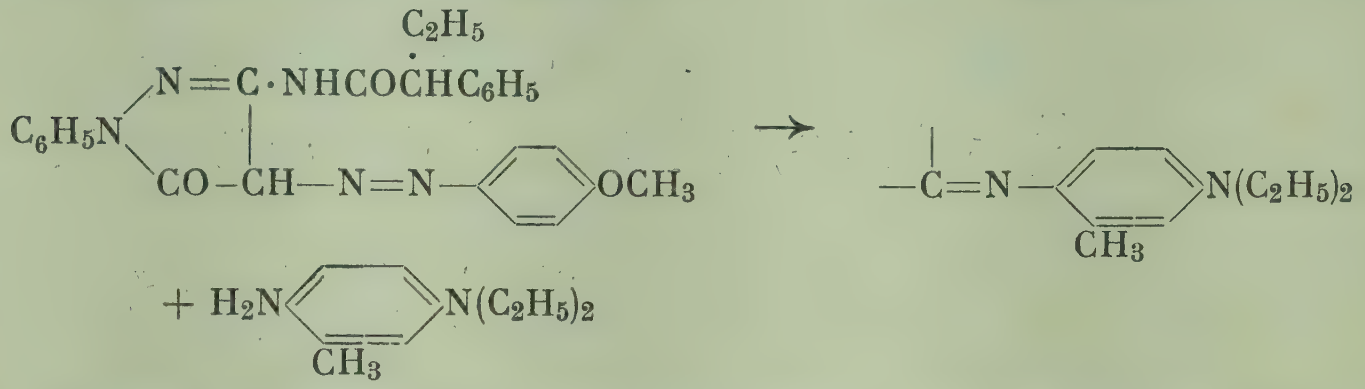
Sym. ureas from monosubst. ureas ←

443. 

(4-Biphenylyl)urea heated at 200-210° for 10 min. → 1,3-di-(4-biphenylyl)urea. Y: 87%. F. e. s. F. Kurzer, Soc. *1949*, 2292.

Silver nitrate *$AgNO_3$*

Azomethines from azo compounds CHN : NR → C : NR′

444. 

A soln. of 1-phenyl-3-(α-phenylbutyramido)-4-(p-anisylazo)-5-pyrrazolone in ethyl acetate stirred with a soln. of Ag-nitrate in aq. NH_3, an aq. soln. of 2-amino-5-diethylaminotoluene hydrochloride added dropwise, and stirring continued for 30 min. → azomethine dye. Y: 66%. F. e. s. P. W. Vittum et al., Am. Soc. *72*, 1533 (1950).

Zinc *Zn*

Formamides from azo compounds ·N : NR → ·NHCHO

s. *6*, 519

Alumina *Al_2O_3*

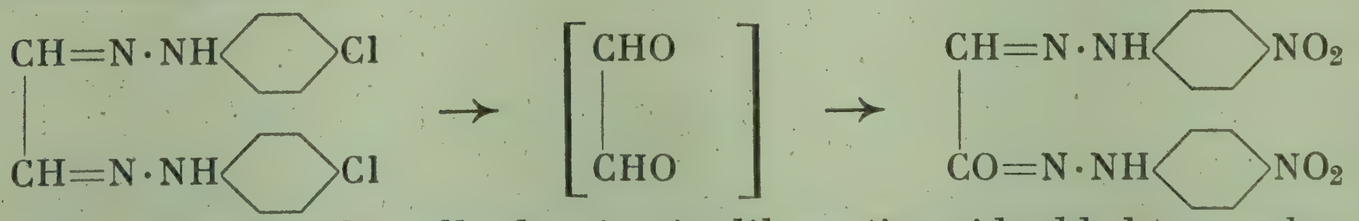
Selfcondensation $2\ RNH_2 \rightarrow R_2NH$

445/6. $2\ C_6H_5NH_2 \rightarrow C_6H_5NHC_6H_5$

Aniline passed at 460° over activated alumina → diphenylamine. Conversion: ca. 35%. Under optimum conditions, because of the absence of side reactions, yields after recycling should approach 100%. H. E. Hoelscher and D. F. Chamberlain, Ind. Eng. Chem. *42*, 1558 (1950); correction s. *43*, 1828 (1951).

Acetic acid *CH_3COOH*

Transosazonation ←

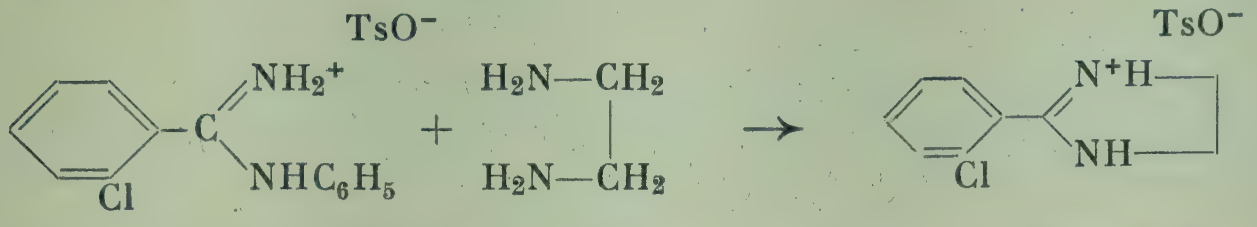
447. 

A soln. of p-nitrophenylhydrazine in dil. acetic acid added to a soln. of glyoxal p-bromophenylosazone in methyl cellosolve, and refluxed 2.5 hrs. on a water bath → glyoxal p-nitrophenylosazone. Y: 87%. F. e. s. I. Mandl, Arch. Biochem. *25*, 109 (1950).

Sulfonates ←

Imidazolines and other 1,3-diazacycloalkenes from subst. amidines ○

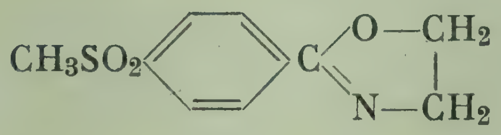
448.



An equimolecular mixture of N-phenyl-o-chlorobenzamidine p-toluenesulfonate and ethylenediamine heated 30 min. at 140° → 2-(o-chlorophenyl)-4,5-dihydroglyoxalinium p-toluenesulfonate. Y: 88%. F. e. s. P. Oxley and W. F. Short, Soc. *1950*, 859.

Δ^2-Oxazolines from α-aminoalcohols

449.



N-Phenyl-p-(methylsulfonyl)benzamidinium benzenesulfonate and 2-hydroxyethylamine heated 4 hrs. on a steam bath → 2-p-methylsulfonylphenyl-Δ^2-oxazoline. Y: 82%. F. e. s. P. Oxley and W. F. Short, Soc. *1950*, 1100.

Sulfuric acid *H_2SO_4*

Azines from ketones via hydrazones ←

450.

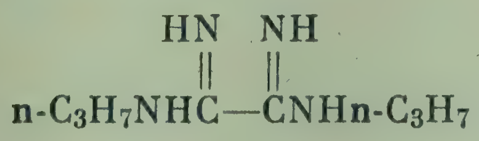
$$2\,(C_6H_5)_2CO + 2\,H_2N\cdot NH_2 \rightarrow 2\,(C_6H_5)_2C{=}N\cdot NH_2$$
$$\rightarrow (C_6H_5)_2{=}N\cdot N{=}C(C_6H_5)_2$$

The reaction of hydrazine with carbonyl compounds proceeds with increasing difficulty as the carbonyl compound varies in the order aldehyde < dialkyl ketone < alkaryl ketone < diaryl ketone.—E: Benzophenone and hydrazine hydrate in 95%-ethanol refluxed 16-24 hrs. in a Soxhlet extractor, the extraction thimble of which is filled with freshly heated CaO → benzophenone hydrazone (Y: 88%) mixed with 95%-ethanol, treated with a few drops of concd. H_2SO_4 until the mixture remains acidic to methyl orange indicator, and allowed to stand 12-15 hrs. → benzophenone azine (Y: 85%). F. e. s. H. H. Szmant and C. McGinnis, Am. Soc. *72*, 2890 (1950).

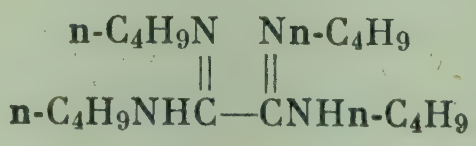
Hydrochlorides ←

Subst. oxamidines ←

451.



$$n\text{-}C_3H_7NH\overset{\overset{HN}{\|}}{C}-\overset{\overset{NH}{\|}}{C}NHn\text{-}C_3H_7$$



$$n\text{-}C_4H_9NH\overset{\overset{n\text{-}C_4H_9N}{\|}}{C}-\overset{\overset{Nn\text{-}C_4H_9}{\|}}{C}NHn\text{-}C_4H_9$$

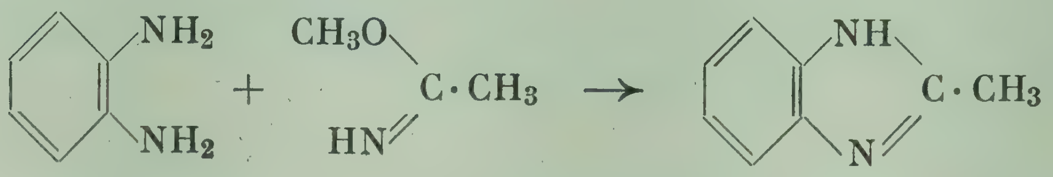
sym-Di-n-propyloxamidine dihydrochloride refluxed 5 hrs. with excess

n-propylamine →	n-butylamine →
sym-tetra-n-propyloxamidine.	*sym*-tetra-n-butyloxamidine.
Y: 80%.	Y: 90%.

In other cases, only the alkyl groups are exchanged, a second disubst. oxamidine resulting thereby. F. e. s. H. Woodburn, B. A. Morehead, and Chen Ming Chih, J. Org. Chem. *15*, 541 (1950).

Imidazole ring from iminoesters ○

452.



A mixture of o-phenylenediamine and acetimino methyl ester hydrochloride in methanol warmed 10 min. on a steam bath → 2-methylbenzimidazole. Y: 91%. F. e. s. F. E. King and R. M. Acheson, Soc. *1949*, 1396; s. a. J. Walker, Soc. *1949*, 2002.

Via intermediates *v.i.*

Subst. carboxylic acid amides from carboxylic acid hydrazides via carboxylic acid azides $CONHNH_2 \rightarrow CONHR$

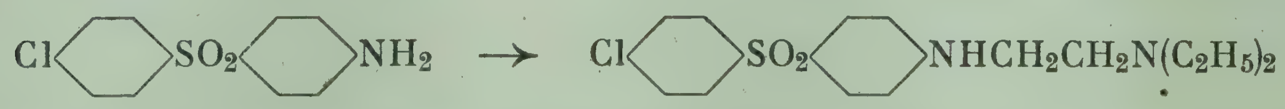
s. *6*, 226; s. a. *1*, 359; Helv. *33*, 57, 108 (1950)

Halogen ↑ NC ⇵ Hal

Without additional reagents *w.a.r.*

Sec. from prim. amines and halides $NH_2 \rightarrow NHR$

453.



Twice the theoretical amount of β-chloroethyldiethylamine added to a warm soln. of p-aminophenyl p-chlorophenyl sulfone in p-dichlorobenzene, and boiled 1 hr. → p-(2-diethylaminoethyl)aminophenyl p′-chlorophenyl sulfone. Y: 75%.—p-Dichlorobenzene was found to be the most suitable of several solvents. F. e., also via sulfonic acid amides, s. E. Knüsli, G. *79*, 621 (1949).

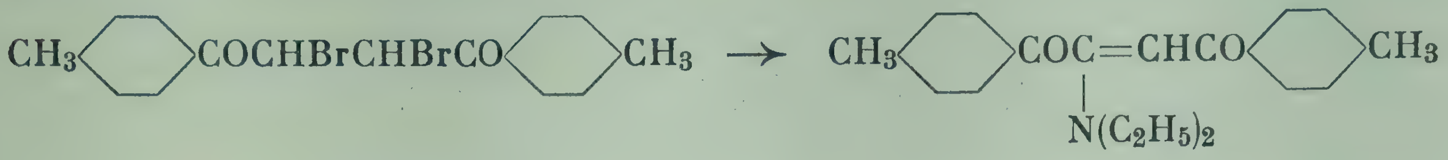
Diamines from halogenamines
Rearrangement of halogenamines

s. *5*, 325; s. a. R. C. Elderfield and C. Ressler, Am. Soc. *72*, 4059 (1950)

Enamines from 1,2-dibromides

$CHBrCHBr \rightarrow CH{:}C{\cdot}N<$

454.



A suspension of 1,2-di-(p-methylbenzoyl)ethylene dibromide in ethanol containing a large excess of diethylamine kept 20-25 min. at 50-65° → 1-diethylamino-1,2-di-(p-methylbenzoyl)ethylene. Y: 90%. F. e. s. R. E. Lutz et al., J. Org. Chem. *15*, 181 (1950).

Isocyanates from amines via carbamyl chlorides

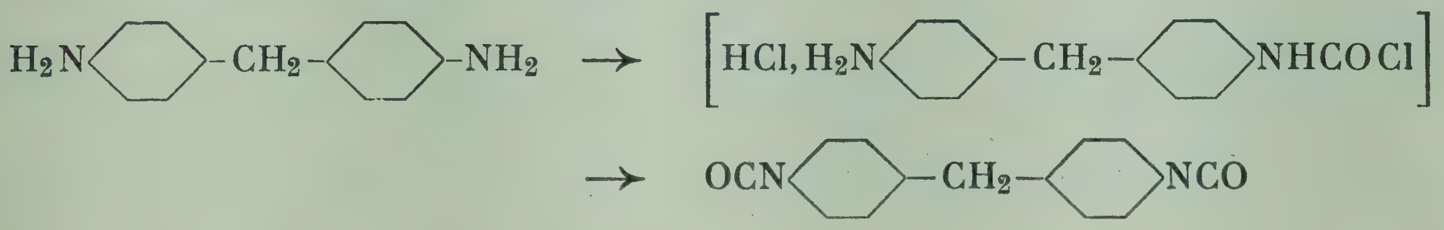
$NH_2 \rightarrow N{:}C{:}O$

455. $CH_3NH_2 + COCl_2 \rightarrow CH_3NHCOCl \rightarrow CH_3N{=}C{=}O$

Methylamine passed with 1.3 mole $COCl_2$ through a Pyrex tube at ca. 275° → crude methylcarbamyl chloride stirred and treated slowly with a soln. of dry pyridine and toluene → methyl isocyanate. Y: 88%. F. e. also without using a tert. amine in the second step, s. R. J. Slocombe et al., Am. Soc. *72*, 1888 (1950).

Di-isocyanates from diamines

456.



A hot soln. of 4,4′-diaminodiphenylmethane in o-dichlorobenzene added to an ice-salt cooled soln. of $COCl_2$ in o-dichlorobenzene so that the temp. does not exceed 0°, the suspension formed slowly heated to 130°, and treated with more $COCl_2$ until dissolved → 4,4-diphenylmethane diisocyanate. Y: 84%. F. e., also with carbamic acids, s. W. Siefken, A. *562*, 75 (1949).

Peptides

$COCl \rightarrow CON<$

s. *1*, 426; s. a. F. W. Dunn and K. Dittmer, J. Biol. Chem. *188*, 263 (1951)

Sulfonic acid hydrazides from chlorides

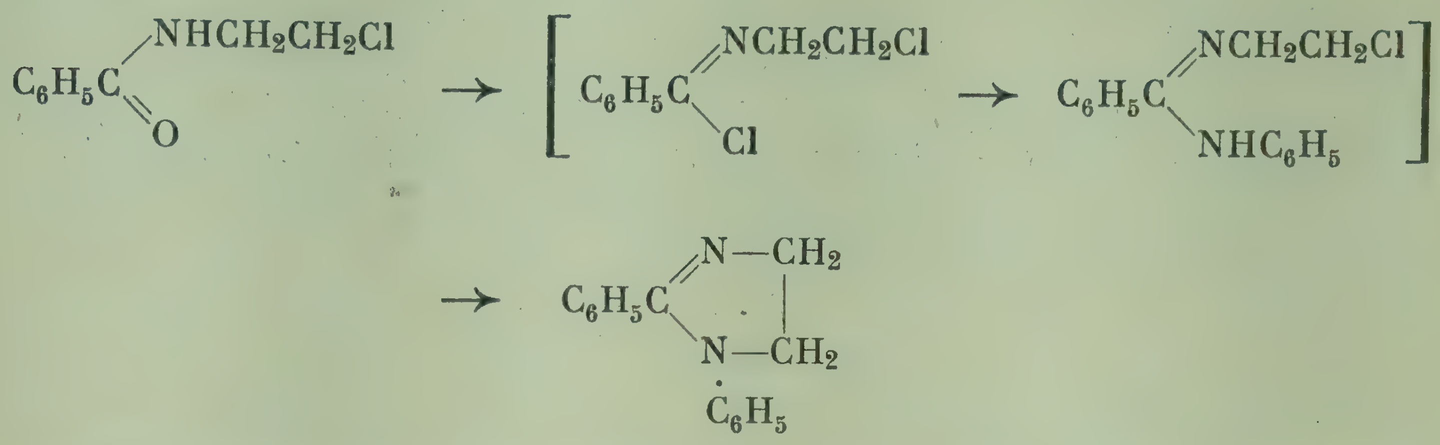
$Cl \rightarrow NHNHSO_2R$

s. *6*, 121

Imidazolines from carboxylic acid amides via iminochlorides and amidines

○

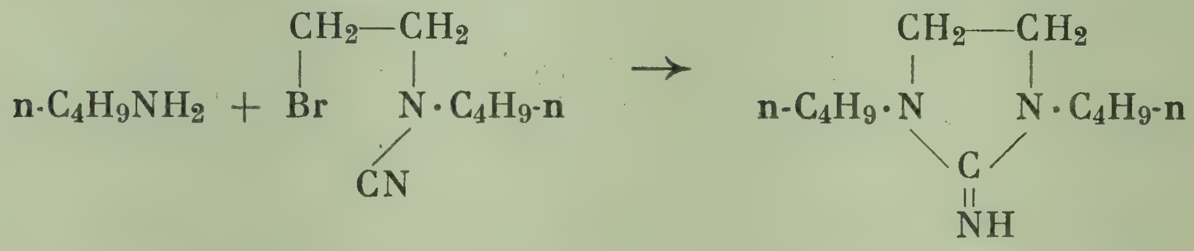
457.



N-2-Chloroethylbenzamide added to a soln. of PCl_5 in dry benzene, to the resulting soln. aniline, dissolved in benzene, added slowly, refluxed for 3 hrs., then the solvent and $POCl_3$ evaporated in vacuo → 1,2-diphenyl-4,5-dihydroglyoxaline. Y: 92%. F. e. s. M. W. Partridge and H. A. Turner, Soc. *1949*, 1308, 3043; amidines from iminochlorides s. a. C. G. Raison, Soc. *1949*, 3319.

Cycl. guanidines from halogenocyanamides

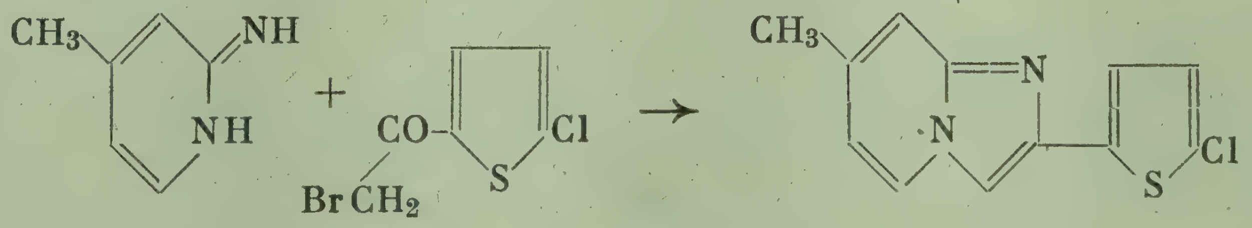
458.



Equimolecular quantities of butyl-β-bromoethylcyanamide and n-butylamine in abs. ethanol refluxed 3-4 hrs. → 1,3-di-n-butyl-2-imino-imidazolidine hydrobromide. Y: 86%. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. *14*, 605 (1949).

Pyrimidazoles

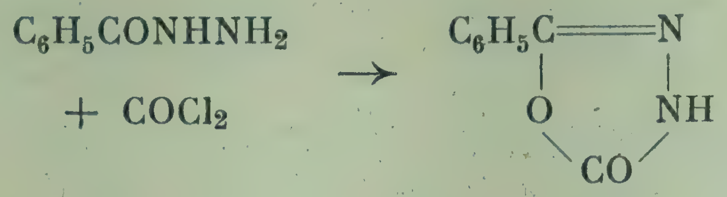
459.



A mixture of 8 gm. 5-chloro-2-bromoacetylthiophene, 4 gm. 4-methyl-2-aminopyridine, and abs. alcohol warmed at 45-50° overnight → 8 gm. 2-(5′-chloro-2′-thienyl)-7-methylpyrimidazole. F. e. s. Ng. Ph. Buu-Hoï and Nguyen-Hoán, R. *68*, 441 (1949).

1,3,4-Oxadiazolones

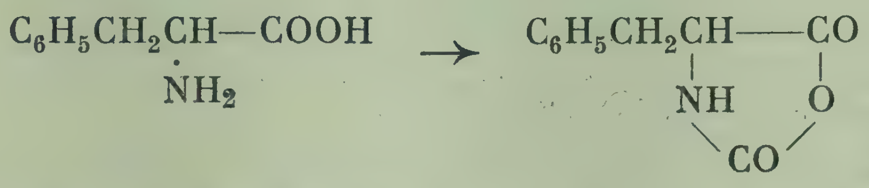
460.



Benzhydrazide in chlorobenzene heated to boiling, then treated with phosgene for 30 min. → 2-phenyl-1,3,4-oxadiazol-5-one. Y: 98%. F. e. and limitations s. T. Lieser and G. Nischk, Chem. B. *82*, 527 (1949).

2,5-Oxazolidiones from α-aminocarboxylic acids

461.



DL-β-Phenylalanine refluxed with a soln. of phosgene in toluene until dissolved → anhydro-N-carboxy-DL-β-phenylalanine. Y: 70%. A. L. Levy, Nature *165*, 152 (1950); Soc. *1950*, 404; s. a. A. C. Farthing, Soc. *1950*, 3213; D. Coleman, Soc. *1950*, 3222; J. L. Bailey, Soc. *1950*, 3461.

Sodium hydroxide *NaOH*

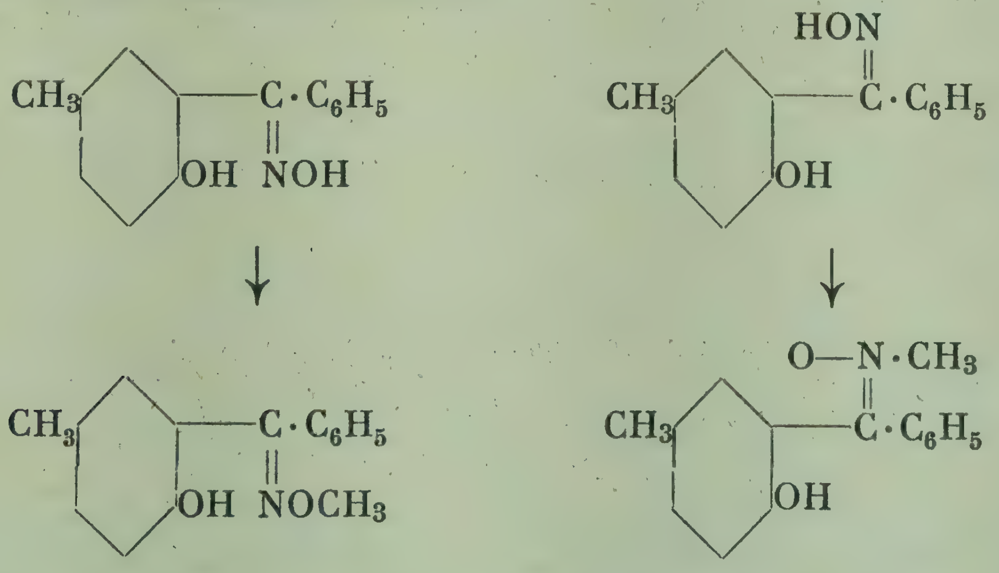
Carbalkoxy derivatives of amines NHCOOR

s. *3*, 368; s. a. H. L. Yale et al., Am. Soc. *72*, 3710 (1950); carballyloxy derivatives s. C. M. Stevens and R. Watanabe, Am. Soc. *72*, 725 (1950); carbobenzoxy derivatives s. S. W. Fox et al., Am. Soc. *72*, 1862 (1950); W. E. Bachmann et al., Am. Soc. *72*, 3132 (1950)

Sodium/alcohol *NaOR*

Alkoximes from isomeric oximes ←

462.



syn- and *anti-*Phenyl 2-hydroxy-5-methylphenyl ketoxime respectively dissolved in 1 mole 1-1.3 *N* Na-methoxide, 1.5-2 mole methyl iodide added, and left stoppered for 18–24 hrs. at room temp.

syn-Ketoxime → *syn*-phenyl 2-hydroxy-5-methylphenyl ketoxime O-methyl ether. Y: 77–83%.

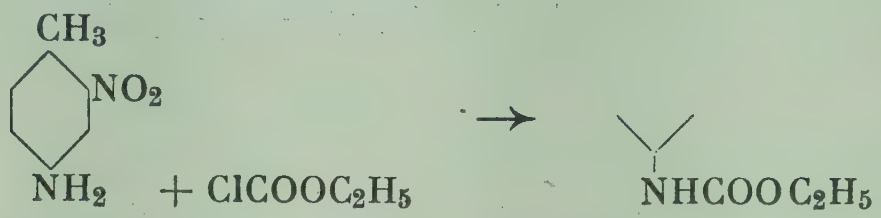
anti-Ketoxime → *anti*-phenyl 2-hydroxy-5-methyl-phenyl ketoxime N-methyl ether. Y: 83-90%.

The difference in the behavior is caused by the H-bond in the *syn*-isomer. A. H. Blatt and S. Archer, Am. Soc. *71,* 3021 (1949).

Carbethoxy derivatives of amines

NHCOOR

463.



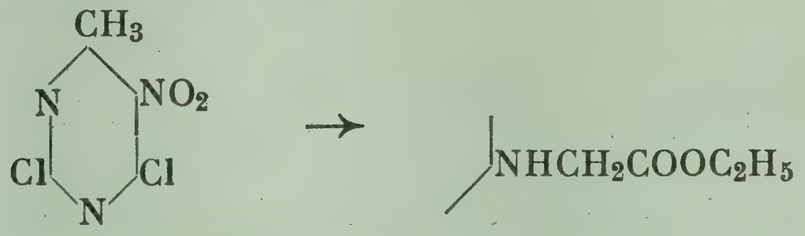
Ethyl chloroformate added slowly with stirring and cooling to a cold soln. of 2-nitro-p-toluidine in abs. alcohol, then Na-ethoxide added so that the mixture is always kept faintly alkaline → N-carbethoxy-2-nitro-p-toluidine. Y: 95%. M. Viscontini and J. Pudles, Helv. *33,* 591 (1950).

Sodium carbonate *Na_2CO_3*

Amines from chlorides
Partial replacement

Hal → NHR

464.

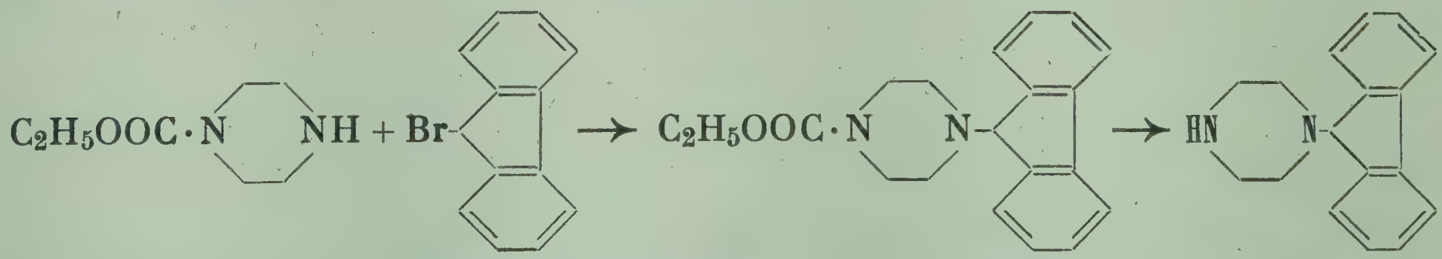


An alc. suspension of glycine ethyl ester hydrochloride added to an alc. suspension of 2,4-dichloro-5-nitro-6-methylpyrimidine, kept 30 min. at 4°, aq. Na-carbonate added with stirring, which is continued for 1.5 hrs. → 4-carbethoxymethylamino-2-chloro-5-nitro-6-methylpyrimidine. Y: 76%.—This partial replacement is made possible by esterification of the carboxylic group of glycine. M. Polonovski and H. Jérôme, C. r. *230,* 392 (1950).

Substitution of piperazines
Elimination of N-carbethoxy groups

NH → NR

465.

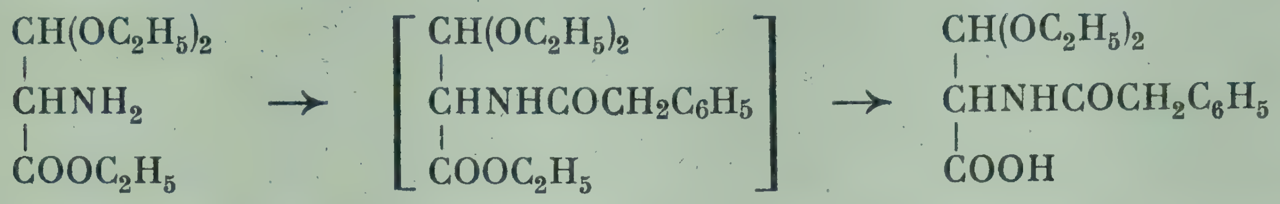


A mixture of 1-carbethoxypiperazine, 9-bromofluorene, and Na-carbonate in butanol heated 4 hrs. on a steam bath → 1-(9-fluorenyl)-4-carbethoxypiperazine (Y: 70%) refluxed 60 hrs. in concd. HCl → 1-(9-fluorenyl)piperazine (Y: 89%). F. e., also disubstitution, and methods, s. K. E. Hamlin et al., Am. Soc. *71,* 2734, 2731 (1949).

Sodium hydrogen carbonate *$NaHCO_3$*

Acylamines from amines $NH_2 \rightarrow NHAc$
Selective hydrolysis

466.



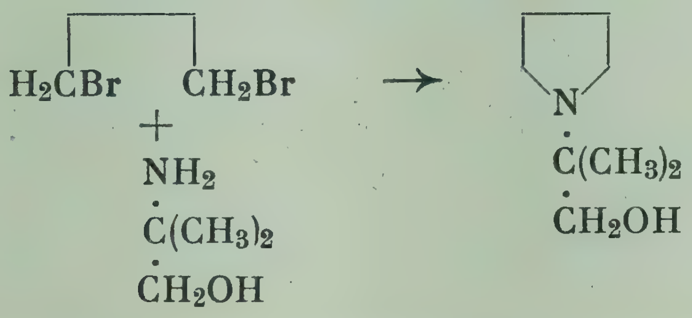
$$\begin{array}{l} CH(OC_2H_5)_2 \\ | \\ CHNH_2 \\ | \\ COOC_2H_5 \end{array} \rightarrow \left[\begin{array}{l} CH(OC_2H_5)_2 \\ | \\ CHNHCOCH_2C_6H_5 \\ | \\ COOC_2H_5 \end{array}\right] \rightarrow \begin{array}{l} CH(OC_2H_5)_2 \\ | \\ CHNHCOCH_2C_6H_5 \\ | \\ COOH \end{array}$$

Phenylacetyl chloride slowly added at 5° to a vigorously stirred mixture of β,β-diethoxyalanine ethyl ester, $NaHCO_3$, water, and chloroform, stirred 1 hr. at room temp., the crude ester obtained added to ethanolic NaOH, and allowed to stand for 5 hrs. → benzylpenaldic acid diethylacetal. Y: 90.7%. F. e. s. E. V. Brown, Chemistry of Penicillin *1949,* 512.

N-Carbethoxyamidines ←
s. *6,* 237

Pyrrolidines from γ-dihalides ○
N-Pyrrolidylalkanols

467.



A mixture of 2-amino-2-methylpropanol, tetramethylene dibromide, and toluene refluxed 3 hrs. with stirring, $NaHCO_3$ added, and refluxed with vigorous stirring for an additional 15 hrs. → 2-(1-pyrrolidyl)-2-methylpropanol. Y: 75.5%. F. syntheses of pyrrolidylalkanols s. R. B. Moffett, J. Org. Chem. *14,* 862 (1949).

Potassium hydrogen carbonate *$KHCO_3$*

Cyanohydrazides CONHNHCN

468. $H_2N \cdot NHCO[CH_2]_4CONH \cdot NH_2 + 2\ BrCN \rightarrow NC \cdot HN \cdot NHCO[CH_2]_4CONH \cdot NH \cdot CN$

Aq. BrCN added to an aq. soln. of adipic acid dihydrazide and $KHCO_3$, and allowed to stand overnight → adipic acid di-(N^β,N'^β-cyanohydrazide). Y: 88%. F. e. s. H. Gehlen, A. *563,* 185 (1949).

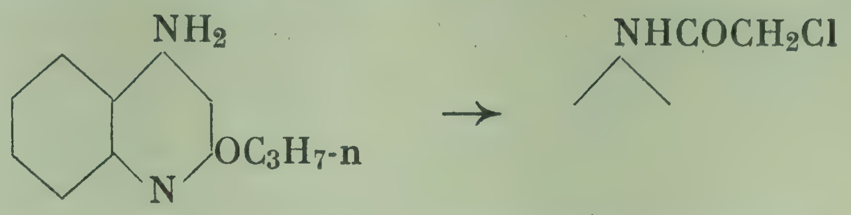
Sodium acetate *CH_3COONa*

α,β-Ethylenehydrazones from α-bromoketones ←

s. *4,* 852; *6,* 891

α-Halogenocarboxylic acid amides CHalCONHR

469.

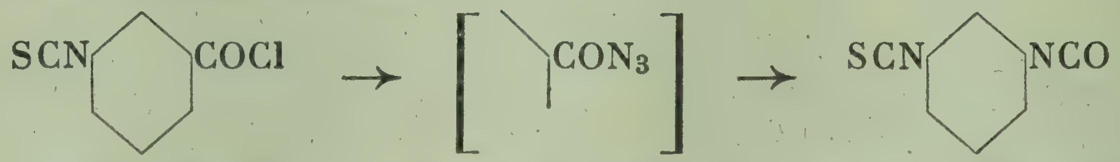


2-n-Propoxy-4-aminoquinoline in acetone treated with anhydrous Na-carbonate, cooled, treated dropwise with chloroacetyl chloride, and boiled 2 hrs. on a water bath → 2-n-propoxy-4-(chloroacetylamino)-quinoline. Y: 90%. F. e. s. J. Büchi, L. Ragaz, and R. Lieberherr, Helv. *32*, 2310 (1949).

Sodium azide NaN_3

Isocyanates from carboxylic acid chlorides via carboxylic acid azides
Activation of sodium azide COCl → N:C:O

470.



3-Isothiocyanobenzoyl chloride refluxed with finely powdered NaN_3 in chlorobenzene for 24 hrs. → 3-isothiocyanophenyl isocyanate. Y: 90%. W. Siefken, A. *562*, 75 (1949); f. activation of NaN_3 s. R. F. Rekker et al., R. *70*, 113 (1951).

Diethylaniline $C_6H_5N(C_2H_5)_2$

Urethans from amines NH → NCOOR

s. *6*, 586

N-Methylmorpholine ←

α-Halogenocarboxylic acid amides CHalCONHR

s. *6*, 308

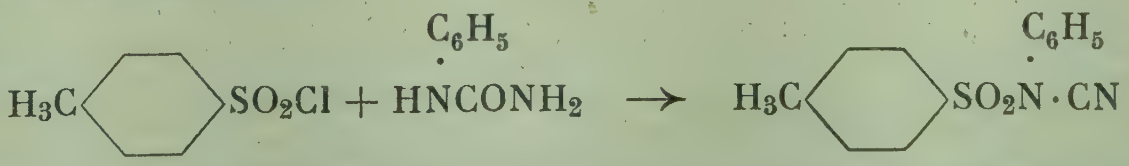
Acylamines from amines and carboxylic acid chlorides NH_2 → NHAc

s. *1*, 374/5; also modified procedure s. P. E. Verkade, B. M. Wepster, and P. H. Witjens, R. *70*, 127 (1951)

Pyridine C_5H_5N

Sulfonylcyanamides from sulfonic acid chlorides SO_2Cl → SO_2NRCN

471.



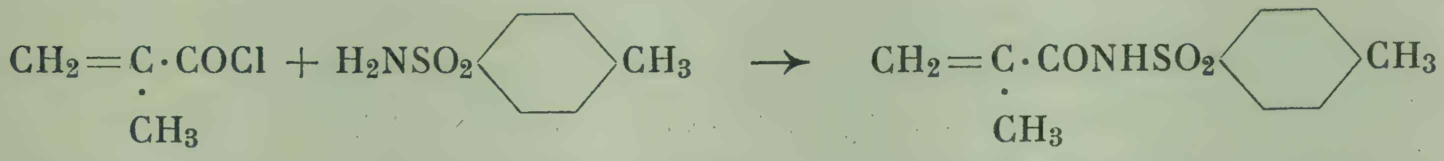
6 mols. p-toluenesulfonyl chloride added with cooling below 30° to a soln. of 1 mol. phenylurea in pyridine, and allowed to stand for 10 min.

→ N-(p-toluenesulfonyl)-N-phenylcyanamide. Y: 95%.—Sulfonylureas, synthesized by alternative methods, are not dehydrated by sulfonyl chlorides under these conditions. F. e. s. F. Kurzer, Soc. *1949*, 1034.

Copper *Cu*

N-Acylsulfonic acid amides SO_2NHAc

472.

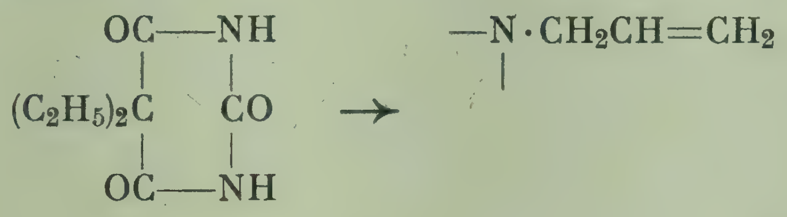


Methacrylyl chloride (prepn. s. 578), p-toluenesulfonamide, and some Cu-powder refluxed ¾ hr. until the HCl-evolution ceases → N-methacrylyl-p-toluenesulfonamide. Y: 75%. F. e. s. J. Heyboer and A. J. Staverman, R. *69*, 787 (1950).

Silver hydroxide *AgOH*

N-Alkylbarbituric acids NH → NR

473.

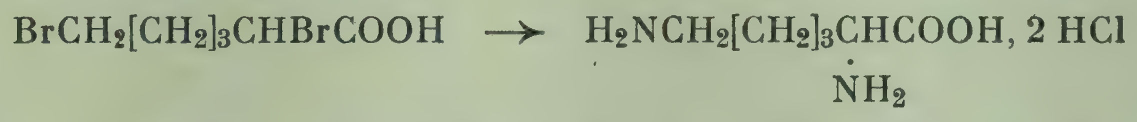


Na-Barbital and allyl chloride refluxed with stirring for 4 hrs. in the presence of AgOH → N-allylbarbital. Y: 87%. A. Halpern and J. W. Jones, J. Am. Pharm. Assoc. *37*, 333 (1948); f. e. s. *38*, 352 (1949).

Cuprous chloride *CuCl*

Prim. amines from halides Hal → NH_2

474.

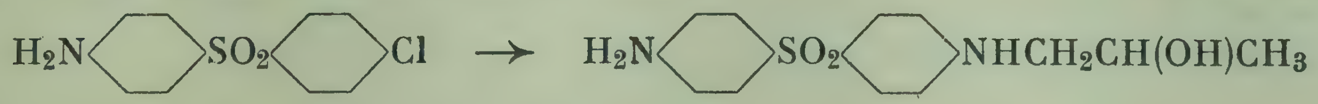


$$BrCH_2[CH_2]_3CHBrCOOH \rightarrow H_2NCH_2[CH_2]_3\underset{NH_2}{CH}COOH,\ 2\,HCl$$

A mixture of 2,6-dibromohexanoic acid, aq. NH_3, NH_4-carbonate, and a little CuCl heated 18-20 hrs. at 125-150° in a closed vessel → lysine dihydrochloride. Y: 81%. F. e. s. D. C. Sayles and E. F. Degering, Am. Soc. *71*, 3161 (1949).

Sec. from prim. amines and halides NH_2 → NHR

475.

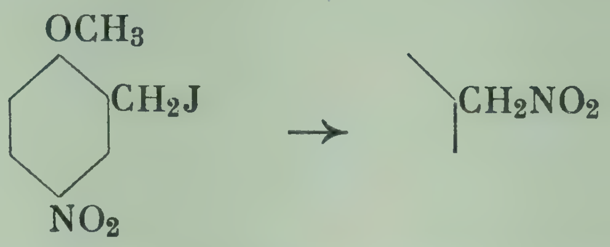


A mixture of 4-amino-4′-chlorodiphenyl sulfone, isopropanolamine, and CuCl stirred and refluxed at 165-175° for 15 hrs., and worked up whereby the copper is removed by treating with H_2S → 4-amino-4′-(β-hydroxypropylamino)diphenyl sulfone. Y: 85%. F. e. s. J. Weijlard and E. F. Swanezy, Am. Soc. *71*, 4134 (1949); s. a. E. C. Hughes, F. Veatch, and V. Elersich, Ind. Eng. Chem. *42*, 787 (1950).

Silver nitrite *$AgNO_2$*

Aliphatic nitro compounds from iodides $I \rightarrow NO_2$

476.

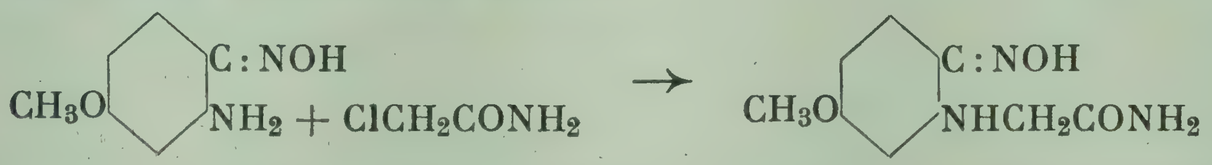


4-Nitro-2-(iodomethyl)anisole in benzene-ether treated with powdered $AgNO_2$, and kept at room temp. for 3 days with occasional shaking → 4-nitro-2-(nitromethyl)anisole. Y: 81%.—$HgNO_2$ gives more hydroxymethyl compound as by-product. G. Bendz et al., Soc. *1950*, 1130.

Calcium carbonate *$CaCO_3$*

Sec. from prim. amines and halides $NH_2 \rightarrow NHR$

477.

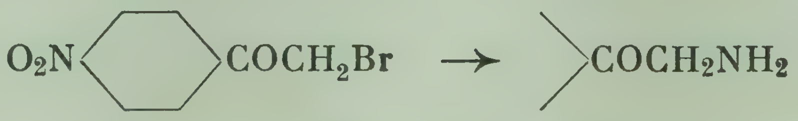


2-Aminoanisaldoxime (prepn. s. 32), Ca carbonate, chloroacetamide, and water refluxed 3 hrs. → 2-formyl-5-methoxyphenylglycineamide oxime. Y: 89%. W. R. Boon, Soc. *1949*, S230.

Hexamethylenetetramine ←

Prim. amines from halides Hal → NH_2

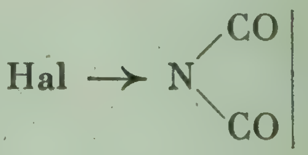
478.



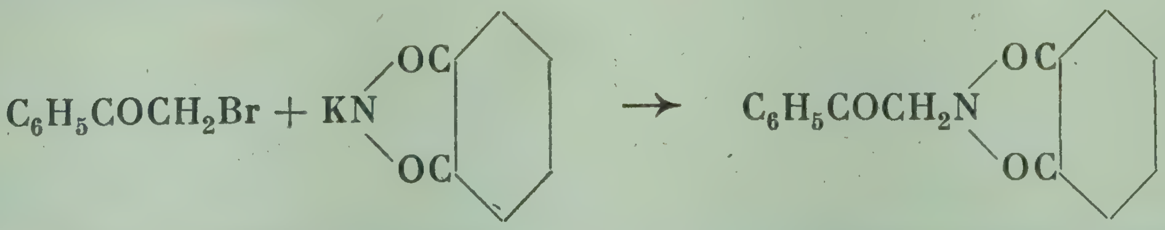
A soln. of p-nitro-α-bromoacetophenone in chlorobenzene added with stirring in one portion at room temp. to a mixture of hexamethylenetetramine and dry chlorobenzene, warmed 4 hrs. at 50-52°, the salt obtained (Y: 95%) added at 25° to a mixture of 95%-ethanol and concd. HCl, and stirred 16 hrs. at room temp. → p-nitro-α-aminoacetophenone hydrochloride. Y: 74%. L. M. Long and H. D. Troutman, Am. Soc. *71*, 2473 (1949); s. a. Ng. Ph. Buu-Hoï et al., Soc. *1950*, 2766.

Dimethylformamide *$HCON(CH_3)_2$*

Phthalimides from halides
Gabriel synthesis
Improved procedure


$Hal \rightarrow N\begin{smallmatrix}CO\\CO\end{smallmatrix}$

479.



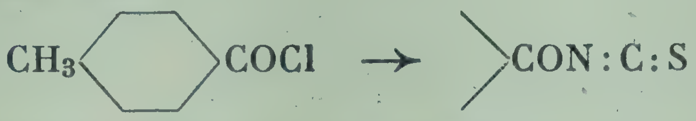
The use of dimethylformamide as solvent for K-phthalimide gives improved yields of the phthalimides.—E: K-phthalimide added to a soln.

of phenacyl bromide in dimethylformamide, and stirring continued for 30 min. → phthalimidoacetophenone. Y: 92%. F. e. s. J. C. Sheehan and W. A. Bolhofer, Am. Soc. *72*, 2786 (1950).

Lead salts *Pb^{++}*

Acylisothiocyanates from carboxylic acid chlorides COCl → CON:C:S

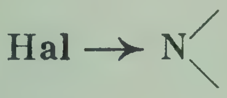
480.



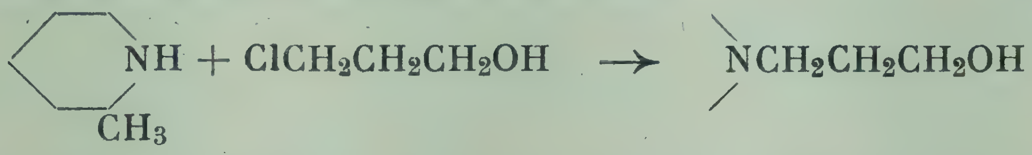
51 gm. p-methoxybenzoyl chloride, benzene, and Pb-thiocyanate boiled with good stirring for 1 hr. → 43 gm. p-methoxybenzoyl isothiocyanate (startg. m. f. 353). F. e. s. E. Hoggarth, Soc. *1949*, 1160.

Alkali iodides *I^-*

(tert-Amino)alcohols from chlorohydrins



481.



A mixture of 2-methylpiperidine, trimethylene chlorohydrin, abs. alcohol, and Na- or K-iodide refluxed with stirring for 24 hrs., cooled, and the stirred mixture treated with a soln. of Na in abs. alcohol → 3-(2-methylpiperidyl-1)-propanol. Y: 92% based on recovered 2-methylpiperidine. F. e. s. R. O. Clinton, U. J. Salvador, and S. C. Laskowski, Am. Soc. *71*, 3366 (1949).

Hydrochlorides ←

Isocyanates from amines NH_2 → N:C:O

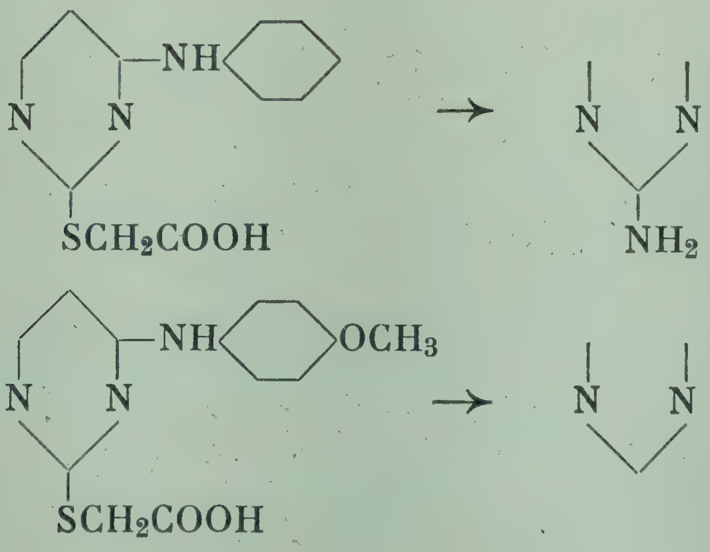
s. *1*, 385; s. a. T. Lieser and G. Nischk, A. *569*, 59 (1950); M. W. Farlow, Org. Synth. *31*, 62 (1951)

Sulfur ↑ NC ↑↓ S

Without additional reagents *w.a.r.*

Carboxymethyl thioethers as intermediates ←

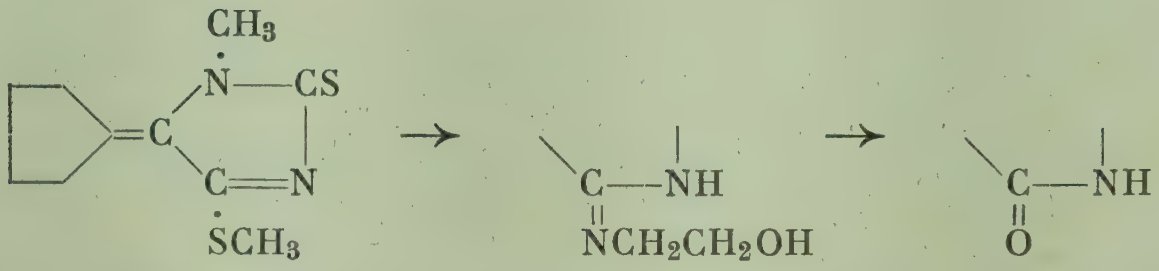
482.



In certain cases replacement of the sulfhydryl group may be best effected via the carboxymethyl derivatives.—E: 4-Anilino-2-(carboxymethylthio)pyrimidine heated with NH_3-soln. (d. 0.9) in a sealed tube at 140-150° for 24 hrs. → 2-amino-4-anilinopyrimidine. Y: 80%.—4-Anilino-2-mercaptopyrimidine gave no reaction under these conditions.—2.2 gm. 4-p-methoxyanilino-2-(carboxymethylthio)pyrimidine refluxed 3 hrs. with Raney-Ni and Na_2CO_3 in abs. alcohol → 1.7 gm. 4-p-methoxyanilinopyrimidine.—The better solubility of the carboxymethyl derivatives may facilitate the desulfuration. F. e. s. G. H. Hitchings and P. B. Russell, Soc. *1949*, 2454.

Oxo compounds from thioenolethers via imines ←

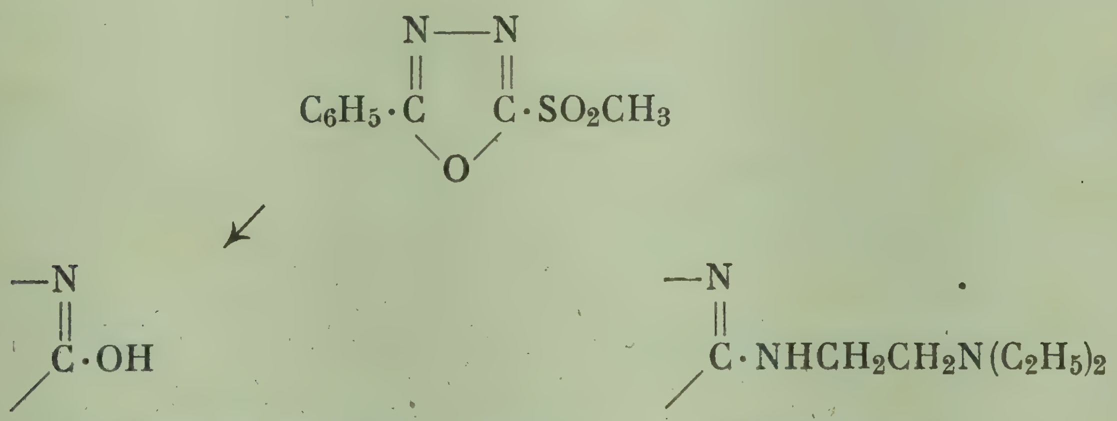
483.



2-Thio-4-methylthio-1-methyl-5,5-pentamethylene-2,5-dihydroglyoxaline and 2-amino-ethanol heated 15 min. at 110-120° → 4-(2′-hydroxyethylimino)-1-methyl-5,5-pentamethylene-2-thiohydantoin (Y: ca. 100 per cent) boiled with 20%-HCl → 1-methyl-5,5-pentamethylene-2-thiohydantoin (Y: 91%). F. e. s. H. C. Carrington and W. S. Waring, Soc. *1950*, 354.

Sec. amines and hydroxy compounds from sulfones ←

484.



2-Methanesulfonyl-5-phenyl-1,3,4-oxadiazole

(1 g.) ground with *N* NaOH → 0.65 g. 2-hydroxy-5-phenyl-1,3,4-oxadiazole.	(3.3 g.) cautiously added to dry 2-diethylaminoethylamine at 80° during 10 min., so that the temp. does not rise above 100° → 3,1 g. 2-(2′-diethylaminoethylamino)-5-phenyl-1,3,4-oxadiazole.

F. e. s. E. Hoggarth, Soc. *1949*, 1918, 3311.

Sodium *Na*

Alkylation of acylamines

NHAc → NRAc

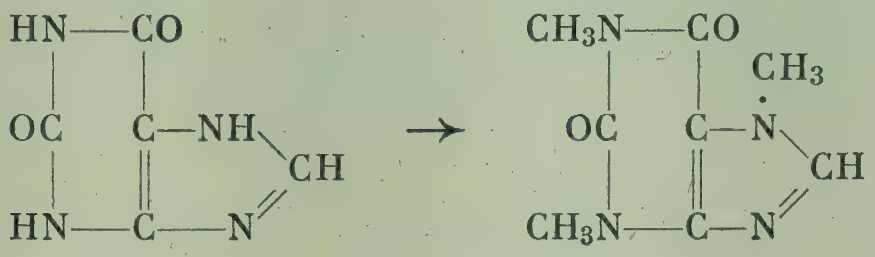
s. *6*, 502

Sodium hydroxide *NaOH*

Methylation of purines

NH → NR

485.



Dimethyl sulfate and NaOH added simultaneously at 35° and pH 8-9 to an aq. suspension of xanthine (prepn. s. 44) over a period of 70 min., and stirring continued for 30 min. at the same pH with addition of a little more aq. NaOH → caffeine. Y: 86-90%.—Depending on the pH, different methylation products are obtained. F. e. s. H. Bredereck, H.-G. v. Schuh, and A. Martini, Chem. B. *83*, 201 (1950).

Acylaminoguanidines from carboxylic acid hydrazides and isothioureas

←

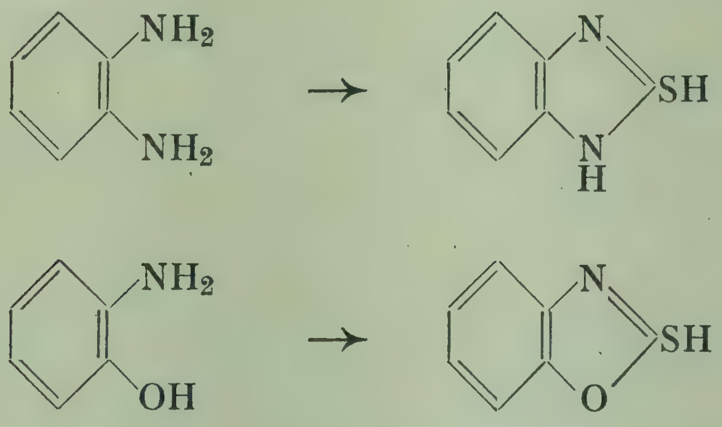
s. *6*, 409

Potassium hydroxide *KOH*

2-Mercaptobenzimidazoles and 2-mercaptobenzoxazoles

○

486.



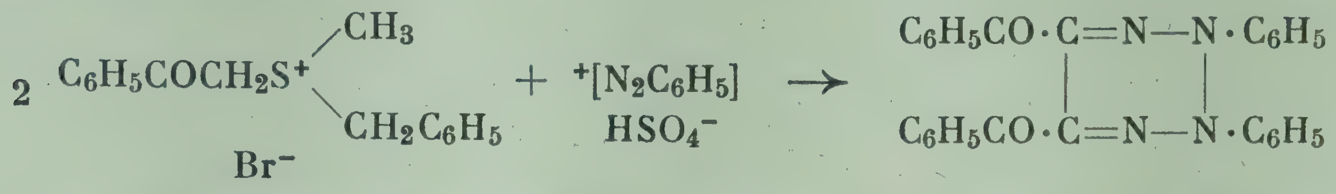
A mixture of o-phenylenediamine, K ethyl xanthate (or KOH and CS_2), ethanol, and water refluxed 3 hrs. → 2-mercaptobenzimidazole. Y: 84 to 86.5%.—Similarly with o-aminophenol → 2-mercaptobenzoxazole. Y: 80%. J. A. Van Allan and B. D. Deacon, Org. Synth. *30*, 56 (1950).

Sodium acetate *CH_3COONa*

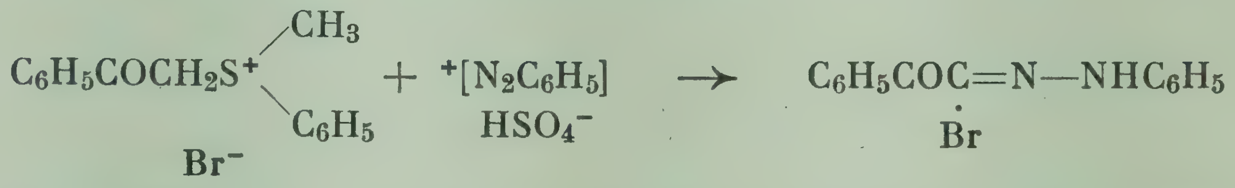
Coupling diazonium salts with sulfonium salts ←

1,2,3,4-Tetrazines

487.



A soln. of methylbenzylphenacylsulfonium bromide and Na-acetate treated with phenyldiazonium sulfate, and allowed to stand overnight → 2,3-diphenyl-5,6-dibenzoyl-2,3-dihydro-1,2,3,4-tetrazine. Crude-Y: 77%.

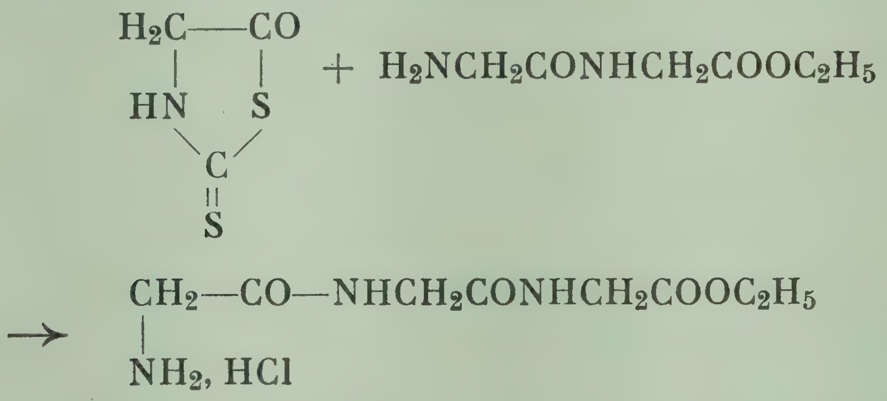


A soln. of 22.7 gm. methylphenylphenacylsulfonium bromide and Na-acetate in 50% methanol treated with phenyldiazonium sulfate, and worked up after 15 min. → 14 gm. crude α-bromo-β-phenylglyoxal α-phenylhydrazone. F. Krollpfeiffer and H. Hartmann, Chem. B. *83*, 90 (1950).

Triethylamine *$(C_2H_5)_3N$*

Peptides from 2-thiazolidinethiones C

488.

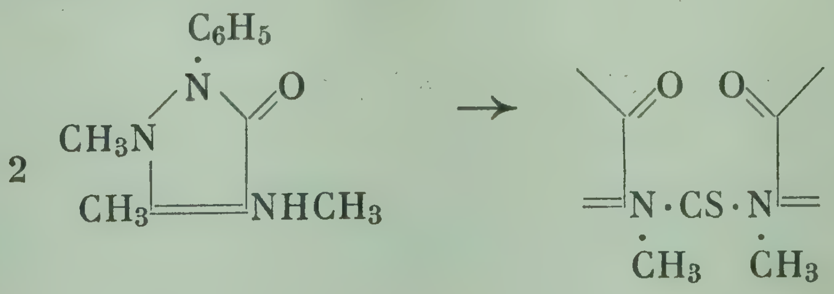


2-Thio-5-thiazolidone added to a mixture of glycylglycine ethyl ester hydrochloride and 2 equivalents of triethylamine in ethanol, and the clear soln. acidified with 5 *N* ethanolic HCl → triglycine ethyl ester hydrochloride. Y: 86%. F. e., methods, and catalysts s. A. H. Cook and A. L. Levy, Soc. *1950*, 646, 651.

Sulfur *S*

Sym. thioureas from amines ←

489.

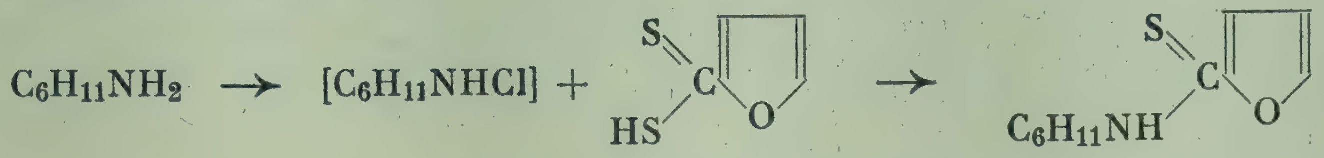


1 gm. 4-methylaminoantipyrine in CS_2 boiled 26 hrs. on a water bath with addition of 4 small portions of S → 1.04 gm. *sym*-diantipyryl-N,N′-dimethylthiourea. F. e. s. J. Halberkann and F. Fretwurst, Z. physiol. Chem. *285*, 97 (1950).

Sodium hypochlorite *NaOCl*

Subst. carboxylic acid thioamides from carbodithioic acids ←

490.

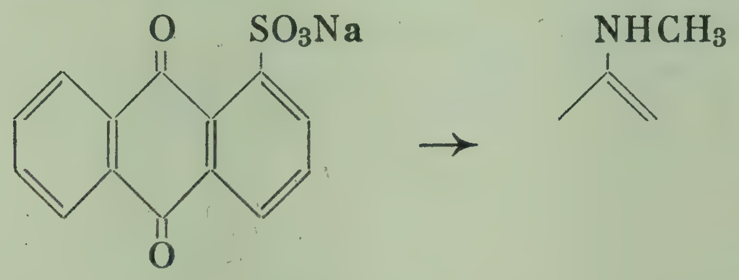


A soln. of dithiofuroic acid in 10%-NaOH soln. added with stirring to a suspension of N-monochlorocyclohexylamine prepared by adding NaOCl to cyclohexylamine with stirring at —10° → N-cyclohexylthiofuramide. Y: ca. 100%. F. e. s. G. Alliger et al., J. Org. Chem. *14*, 962 (1949).

Sodium chlorate *$NaClO_3$*

Sec. from prim. amines and sulfonic acids $SO_3H \rightarrow NHR$

491.



Na- or K-Anthraquinone-α-sulfonate, $NaClO_3$, methylamine, and water heated with stirring in an autoclave at 130-135° for 12 hrs. — 1-methylaminoanthraquinone (startg. m. f. 564). Y: 56-87% depending on the purity of the starting material. C. V. Wilson, J. B. Dickey, and C. F. H. Allen, Org. Synth. *29*, 66 (1949).

Carbon ↑ NC ⇅ C

Without additional reagents *w.a.r.*

Exchange of substituents in ureas ←

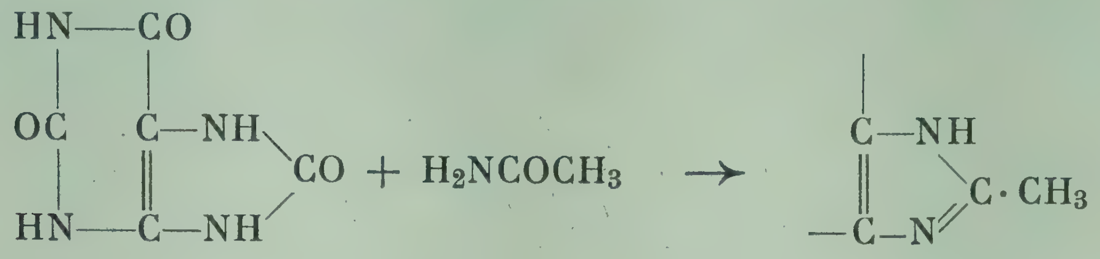
492. $(C_6H_5NH)_2CO + 2\,H_2NCH_2C_6H_5 \rightarrow (C_6H_5CH_2NH)_2CO$

N,N′-Diphenylurea heated with 2 moles benzylamine in tetraline at 180° for 4 hrs. → N,N′-dibenzylurea. Crude Y: ca. 100%.—The higher the basicity of the reacting amine, the greater is the extent of the exchange. F. e. s. M. P. Gerchuk, D. A. Livshits, and S. Z. Taĭts, Ж. *20*. 924 (1950); C. A. *44*, 9444d.

Imidazole ring from imidazolone ring
Purines

←

493.

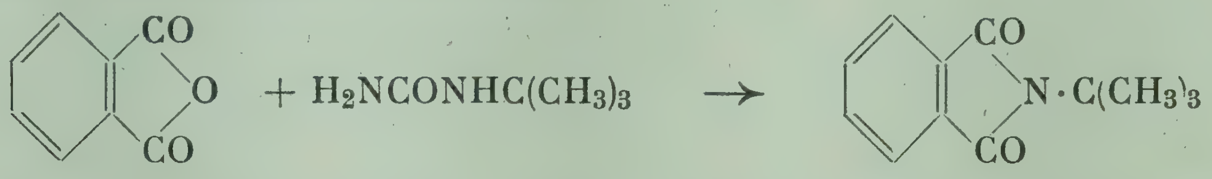


15 gm. uric acid boiled 2 hrs. with 300 gm. acetamide → 12 gm. 8-methylxanthine. F. e., also with formamide, s. H. Bredereck, H. v. Schuh, and A. Martini, Chem. B. *83*, 201 (1950).

N-Subst. phthalimides from ureas

←

494.

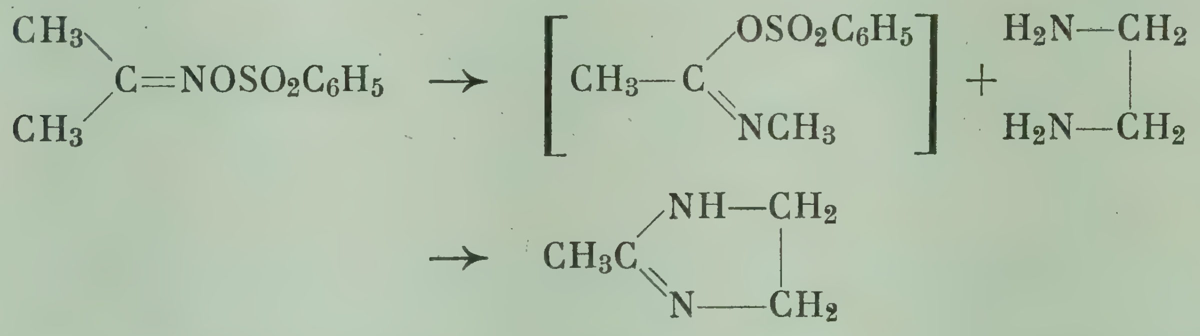


A mixture of *tert*-butylurea (prepn. s. 433) and phthalic anhydride heated 10 min. at 200°, then 5 min. at 220-240° → *tert*-butylphthalimide. Y: 72-76%. F. e. s. L. I. Smith and O. H. Emerson, Org. Synth. *29*, 19 (1949).

Imidazolines from ketoxime sulfonates

○

495.



Acetoxime benzenesulfonate, ethylenediamine, and toluene refluxed 0.5 hr. → 2-methyl-4,5-dihydroglyoxaline. Y: 74.5%, isolated as picrate. F. e. s. P. Oxley and W. F. Short, Soc. *1950*, 859.

Amino-dithiocarbamic acids from imidazolines

←

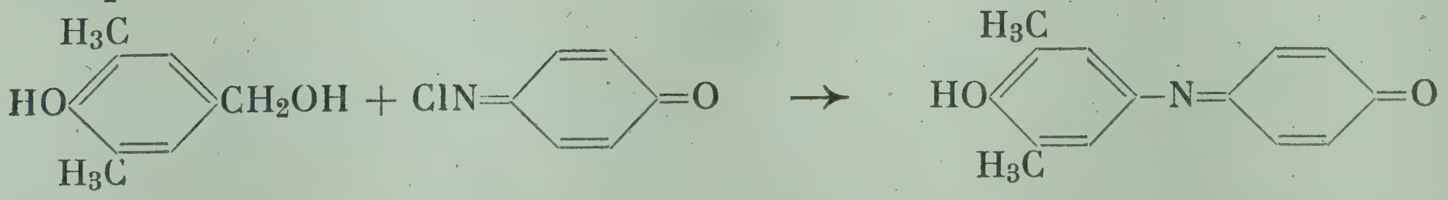
s. *6*, 616

Sodium hydroxide *NaOH*

Indophenols

←

496.



The formation of indophenols may occur even when the position para to the hydroxyl group is substituted.—E: 10%-aq.-NaOH added with stirring at 0° to a suspension of 4-hydroxy-3,5-dimethylbenzylalcohol and p-quinoneimine chloride, and the Na-salt obtained decomposed with CO_2 → 3′,5′-dimethylindophenol. Y: ca. 100%. F. e. s. E. Ziegler and K. Gartler, M. *80*, 759 (1949).

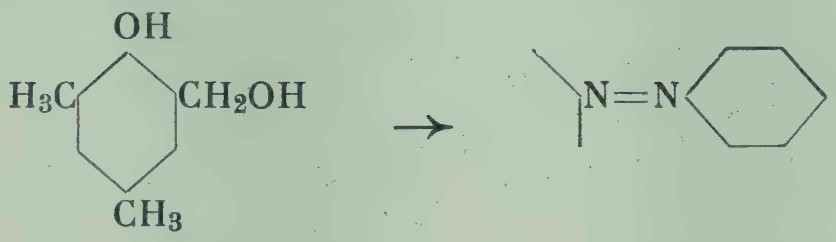
Japp-Klingemann reaction ←
Hydrazones from diazonium salts
α-Ketocarboxylic acid ester phenylhydrazones from β-ketocarboxylic acid esters

s. *2*, 426; s. a. V. Boekelheide and C. Ainsworth, Am. Soc. *72*, 2132 (1950)

Azo compounds by coupling with elimination of formaldehyde

$CH_2OH \rightarrow N:NR$

497.



Benzenediazonium sulfate soln. added with ice-cooling to a soln. of 1.52 gm. 2-hydroxy-3,5-dimethylbenzyl alcohol in 10%-NaOH → 1.6 gm. crude 2-hydroxy-3,5-dimethylazobenzene. F. e. s. E. Ziegler and G. Zigeuner, M. *79*, 42, 89, 358 (1948).

Sodium/alcohol *NaOR*

α-Oximinocarboxylic acid esters from malonic acid esters

$CH(COOR)_2 \rightarrow C(:NOH)COOR$

s. *6*, 823

Sodium acetate CH_3COONa

Hydrazones from diazonium salts
Japp-Klingemann reaction ←

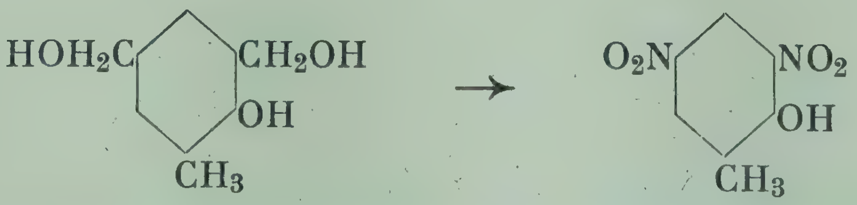
s. *6*, 290

Sodium nitrite $NaNO_2$

Replacement of hydroxymethyl by nitro groups

$CH_2OH \rightarrow NO_2$

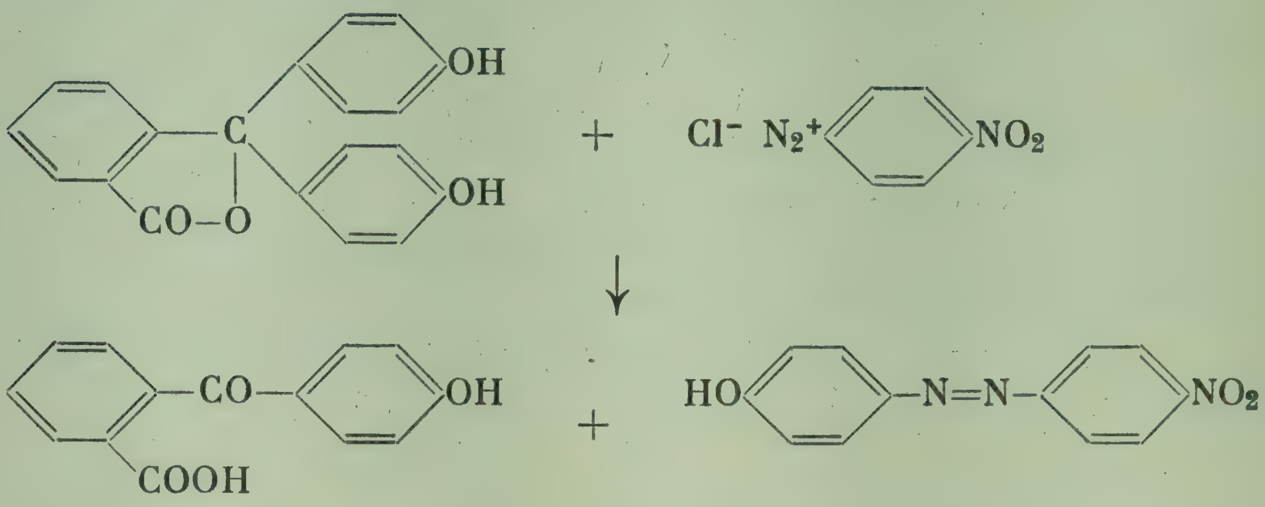
498.



1.68 gm. o-cresoldialcohol allowed to stand 24 hrs. in a soln. of $NaNO_2$ in aq. HCl, then steam-distilled → 1.42 gm. 2,4-dinitro-o-cresol. F. e., also partial replacement, s. E. Ziegler and K. Gartler, M. *80*, 634 (1949).

Cleavage of di- and tri-arylmethane derivatives to azo compounds

499.



A soln. of phenolphthalein in aq. NaOH slowly treated with an equimolecular quantity of p-nitrobenzenediazonium chloride (prepared from p-nitroaniline, $NaNO_2$, and HCl), then neutralized cautiously with dil. H_2SO_4 → 2-(4′-hydroxybenzoyl)benzoic acid (Y: 80%) and 4-(4′-nitrobenzeneazo)phenol (Y: 80%). G. Zigeuner and E. Ziegler, M. *79*, 371 (1948); cleavage of diarylmethane derivatives s. M. *79*, 363 (1948); *80*, 295 (1949).

Hydrazoic acid *HN_3*

Schmidt reaction
Amines from carboxylic acids
Degradation with loss of 1 C-atom

COOH → NH_2

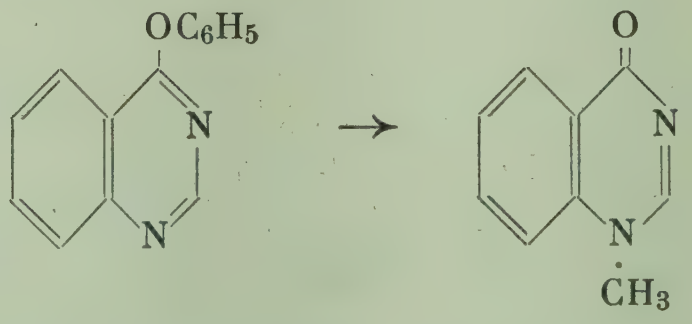
s. *1*, 338/9; *5*, 354; diamines s. D. M. Hall, S. Mahboob, and E. E. Turner, Soc. *1950*, 1842

Tosylates *TsOR*

1-Subst. quinazolones from 4-alkoxyquinazolines

←

500.

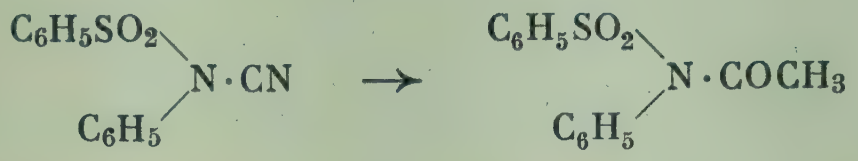


A mixture of 4-phenoxyquinazoline (prepn. s. 244) and methyl p-toluenesulfonate fused at 150° for ¼ hr. → 1-methyl-4-quinazolone (isolated as picrate). Y: 87%. J. S. Morley and J. C. E. Simpson, Soc. *1949*, 1354.

Sulfuric acid *H_2SO_4*

N-Sulfonylcarboxylic acid amides from N-sulfonylcyanamides ←

501.



A soln. of benzenesulfonylphenylcyanamide in acetic anhydride treated with 6 drops of H_2SO_4, and refluxed 2 hrs. → N-acetylbenzenesulfonanilide. Y: 80%. F. e. s. F. Kurzer, Soc. *1949*, 3029.

Hydrochlorides ←

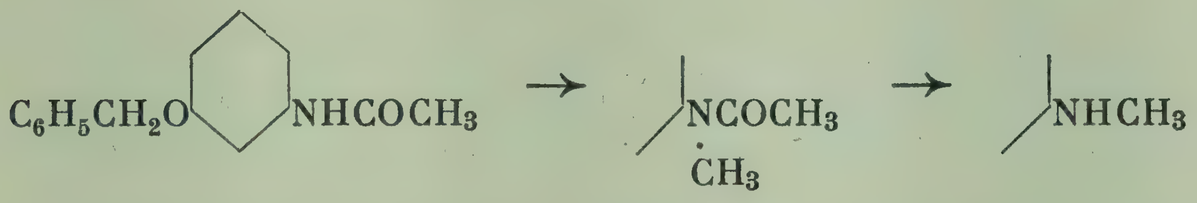
Subst. oxamidines ←

s. *6*, 451

Via intermediates *v.i.*

Sec. amines from acylamines NHAc → NHR

502.



Pure dry m-benzyloxyacetanilide added with rapid stirring at 61° to Na-sand in xylene, the temp. raised to 100-110°, held at this temp. for 1 hr., dry dimethyl sulfate added in small portions without external heating, when the exothermic reaction has subsided stirred an additional 15 min., and worked up, whereby the anilide is hydrolyzed by refluxing with KOH in 90%-alcohol for 48 hrs. → N-methyl-m-benzyloxyaniline. Crude Y: 94%. A. A. Morton and W. R. Slaunwhite, Jr., J. Biol. Chem. *179*, 259 (1949).

Shortened Curtius degradation Amines from carboxylic acids via carboxylic acid chlorides and azides COOH → NH_2

s. *1*, 390; *2*, 466; *3*, 402; *4*, 451; s. a. A. McCoubrey, Soc. *1950*, 1833; H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. *73*, 1414 (1951); compounds with isotopes s. E. M. Gal, R. E. Spenger, and D. M. Greenberg, J. Org. Chem. *15*, 1261 (1950)

Elimination

Hydrogen ↑ NC ⇑ H

Mercuric oxide *HgO*

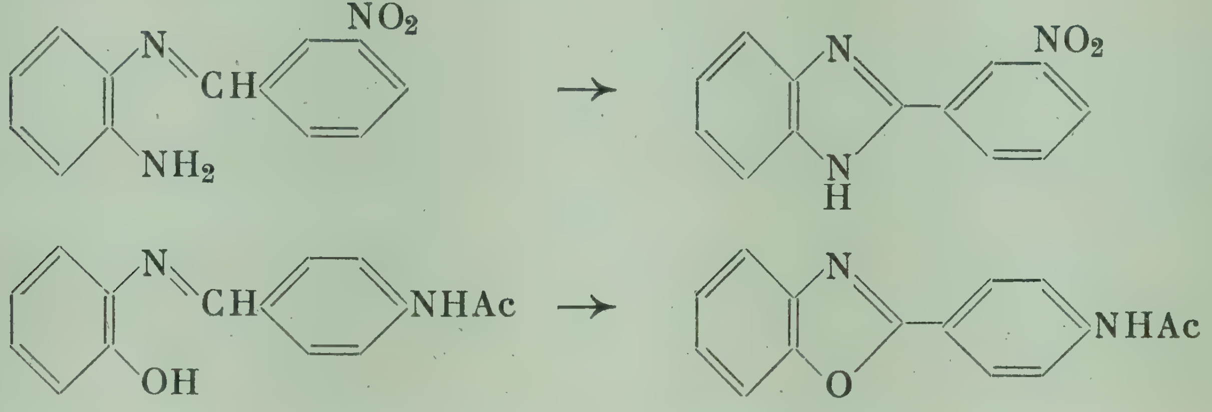
Subst. oximes
from subst. hydroxylamines ←

s. *3*, 403; s. a. A. C. Cope and A. C. Haven, Jr., Am. Soc. *72*, 4896 (1950)

Lead tetraacetate *$(CH_3COO)_4Pb$*

Benzimidazoles and benzoxazoles
from azomethines ○

503.



Benzimidazoles and benzoxazoles are obtained in excellent yields by treatment of the corresponding Schiff's base, in benzene or acetic acid, with 1 molecular equivalent of Pb-tetraacetate.—E: N-m′-Nitrobenzylidene-o-phenylenediamine → 2-m-nitrophenylbenzimidazole. Y: 95%. —2-(p-acetamidobenzylideneamino)phenol → 2-p-acetamidophenylbenzoxazole. Y: 95%. F. e. s. F. F. Stephens and J. D. Bower, Soc. *1949*, 2971. Other reagents, particularly chloranil, N-bromosuccinimide, and benzoyl peroxide, can be used as well. Soc. *1950*, 1722.

Hydrogen peroxide *H_2O_2*

Quinoxalines from
1,2,3,4-tetrahydroquinoxalines ←

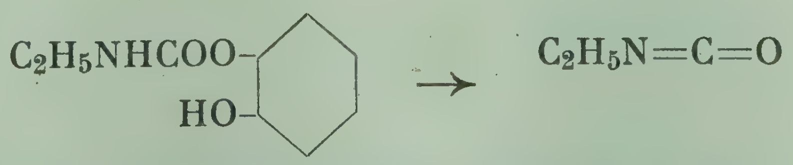
s. *6*, 514

Oxygen ↑ NC ⇑ O

Without additional reagents *w.a.r.*

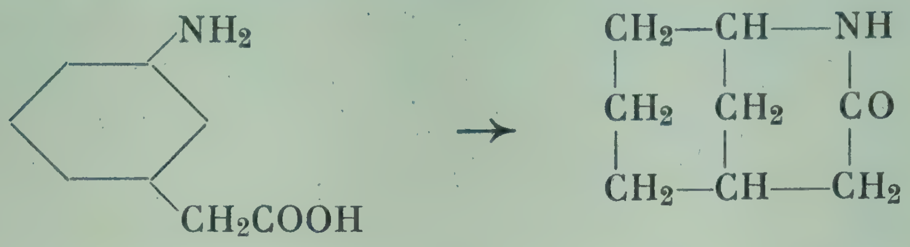
Low molecular isocyanates
from urethans NHCOOR → N:C:O

504.



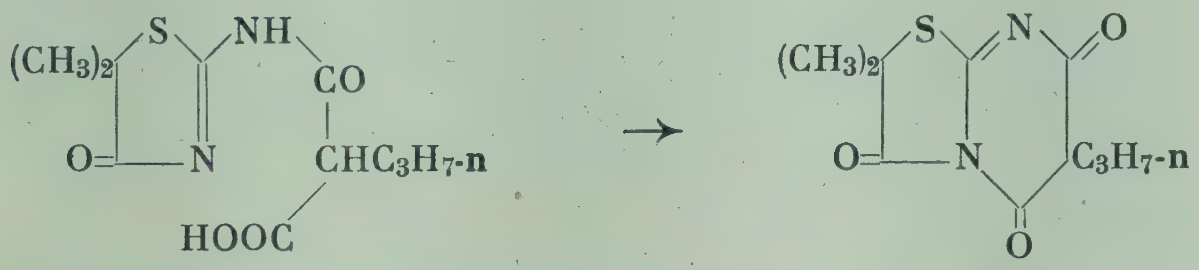
Pyrocatechol mono(ethylcarbamate) (prepn. s. 341) distilled at 210 to 250° → ethyl isocyanate. Y: 40-55%. F. e. s. S. Petersen, A. *562*, 205 (1949).

m-Ring closure of N-heterocyclics ○

505.


cis-3-Aminocyclohexaneacetic acid heated in an N_2-atmosphere for 30 min. at 260° → *cis*-3-aminocyclohexaneacetic acid lactam (startg. m. s. 636). Y: 90%. F. e. s. M. W. Cronyn, J. Org. Chem. *14*, 1013 (1949).

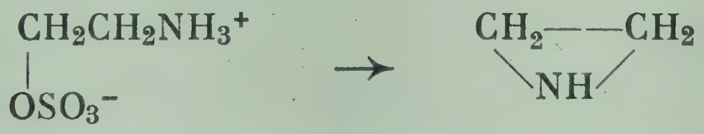
Thiazolo[3.2-a]pyrimidines, 2,3,6,7-tetrahydro-

506.


0.5 gm. 2-(α-carboxy-n-valerylamido)-5,5-dimethyl-4-thiazolone heated 2 hrs. at 185°/0.001 mm. → 0.4 gm. 3,5,7-triketo-2,2-dimethyl-6-n-propyl-2,3,6,7-tetrahydro-5*H*-thiazolo[3.2-a]pyrimidine. F. e. s. P. J. Heald and T. K. Walker, Soc. *1950*, 1127.

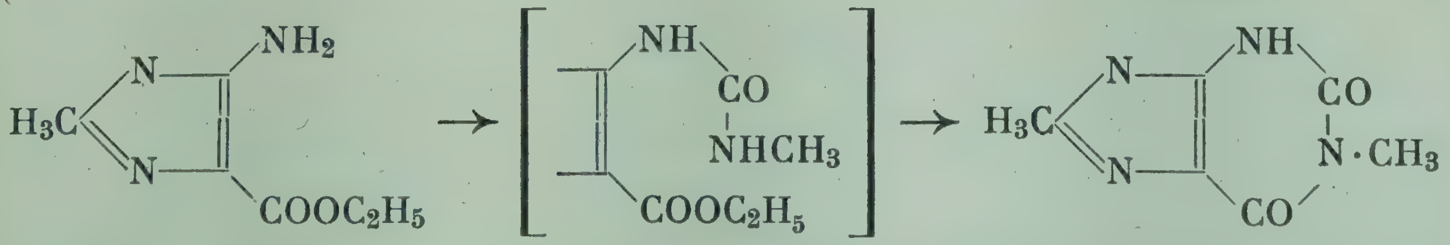
Sodium hydroxide *NaOH*

Cyclic imines from aminosulfuric acid esters

507.


A mixture of β-aminoethylsulfuric acid and 40%-NaOH heated to boiling with a free flame, and after the reaction has subsided, heating resumed, and the mixture distilled as quickly as possible → ethyleneimine. Y: 34-37%. C. F. H. Allen, F. W. Spangler, and E. R. Webster, Org. Synth. *30*, 38 (1950).

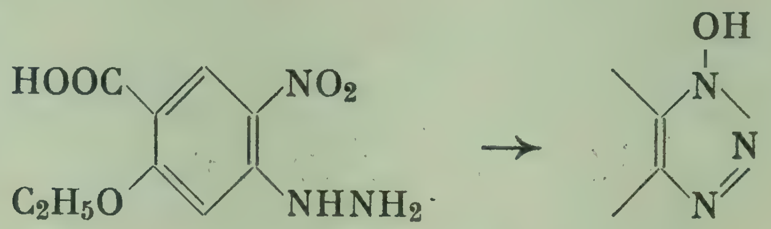
Pyrimidine ring
New synthesis of purines from imidazoles
Thiazolo[5.4-d]pyrimidines

508.


4-Amino-5-carbethoxy-2-methylglyoxaline and a large excess of methyl isocyanate in pyridine refluxed 2 hrs., pyridine removed in vacuo, and the residue boiled with 10%-NaOH → 1,8-dimethylxanthine. Y: 67%. F. e., also isolation of the intermediate, s. A. H. Cook et al., Soc. *1949*, 1071; thiazolo[5,4-d]pyrimidines from thiazoles s. Soc. *1949*, 1064, 1069.

1,2,3-Triazoles

509.

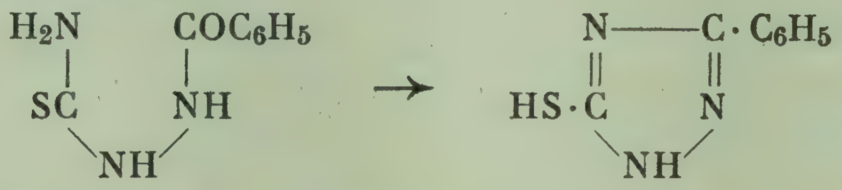


5-Nitro-4-hydrazino-2-ethoxybenzoic acid (prepn. s. 442) dissolved in 2 *N* NaOH, and heated 1 min. on a steam bath → 6-ethoxy-3-hydroxybenzotriazole-5-carboxylic acid. Y: 96%. H. Goldstein and R. Brochon, Helv. *32*, 2334 (1949); with Na-carbonate s. Helv. *34*, 146 (1951).

Sodium/alcohol *NaOR*

1,2,4-Triazoles from acylthiosemicarbazides

510.



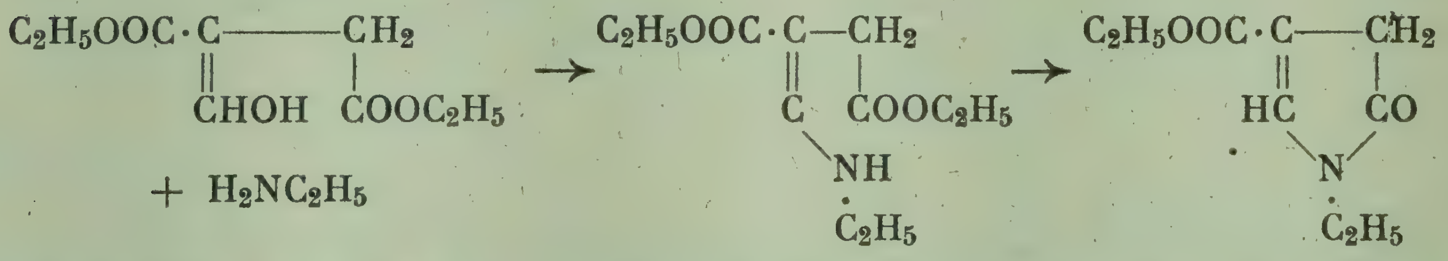
3.9 gm. 1-benzoylthiosemicarbazide added to a soln. of Na in alcohol, then gently refluxed for 12 hrs. → 2.8 gm. 3-phenyl-1,2,4-triazole-5-thiol. F. e. s. E. Hoggarth, Soc. *1949*, 1163, 1160; *1950*, 614, 1579.

Potassium/alcohol *KOR*

2-Pyrrolines

α-Aminomethylene compounds from α-hydroxymethylene compounds

511.



An ethereal soln. of ethylamine, obtained from the hydrochloride with concd. aq. KOH, mixed with diethyl formylsuccinate, and allowed to stand for 2 hrs. → diethyl ethylaminomethylenesuccinate (Y: 91%) dissolved in abs. benzene, then dropped under anhydrous conditions in a stream of N_2 into a cold soln. of K in tert.-amyl alcohol-benzene with swirling, and allowed to stand overnight → 1-ethyl-4-carbethoxy-2-pyrrolone (Y: 75%). F. e. s. C. A. Grob and P. Ankli, Helv. *32*, 2010 (1949); α-aminomethylene from α-hydroxymethylene compounds s. a. A. H. Cook et al., Soc. *1950*, 1947.

1,2-Dihydroimidazo[1.2-a]pyrroles via α-aminopyrroles from aminomethylene compounds
s. *6*, 374

Sodium carbonate Na_2CO_3

1,2,3-Triazoles
s. *6*, 509

Pyridine C_5H_5N

Disubst. cyanamides from ureas $R_2NCONH_2 \rightarrow R_2NCN$

512. $(C_6H_5)_2NCONH_2 \rightarrow (C_6H_5)_2NC{\equiv}N$

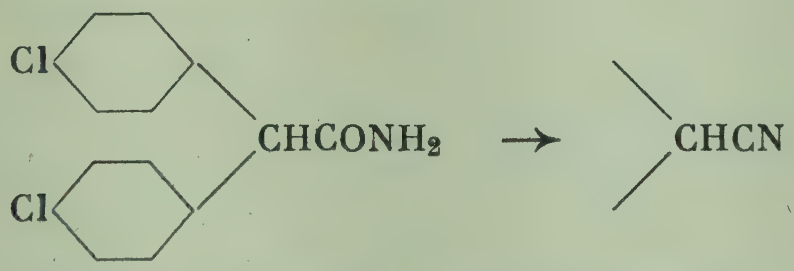
A soln. of *as*-diphenylurea in pyridine treated with excess p-toluenesulfonyl chloride, and heated 2 hrs. on a steam bath → diphenylcyanamide. Y: 97%. F. Kurzer, Soc. *1949*, 3033.

N-Sulfonylcyanamides from ureas ←
s. *6*, 333

Acetic anhydride $(CH_3CO)_2O$

Nitriles from carboxylic acid amides $CONH_2 \rightarrow CN$

513.

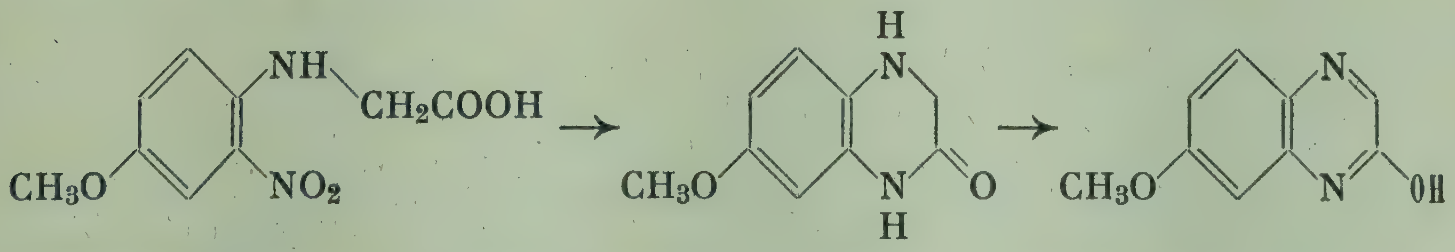


1,1-Bis-(p-chlorophenyl)acetamide refluxed 4 hrs. with acetic anhydride → 1,1-bis-(p-chlorophenyl)acetonitrile. Y: 89%. P. Weiss, M. G. Cordasco, and L. Reiner, Am. Soc. *71*, 2650 (1949).

Tin *Sn*

Quinoxalines via 1,2,3,4-tetrahydroquinoxalines ○
Reductive ring closure

514.



Concd. HCl added in small portions to a mixture of N-(2-nitro-4-methoxyphenyl)glycine, Sn, and ethanol, then refluxed 2 hrs. → 1,2,3,4-tetrahydro-2-keto-7-methoxyquinoxaline (Y: 85%) and H_2O_2 in aq.

NaOH heated 2 hrs. on a steam bath → 2-hydroxy-7-methoxyquinoxaline (Y: ca. 100%). F. e. s. R. L. Wear and C. S. Hamilton, Am. Soc. *72,* 2893 (1950).

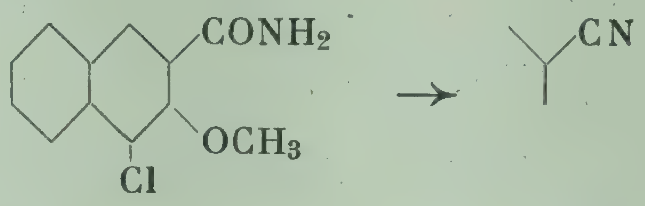
Phosphorus oxychloride *$POCl_3$*

Nitriles from carboxylic acid amides $CONH_2 \rightarrow CN$

s. *3,* 407; s. a. E. J. Skerrett and D. Woodcock, Soc. *1950,* 2718

Phosphorus pentachloride *PCl_5*

515.



4-Chloro-3-methoxynaphthoic acid amide heated with an equal amount of PCl_5 in a water bath until the evolution of HCl ceases → 4-chloro-3-methoxy-2-naphthonitrile. Y: 90%. F. e. s. H. Richtzenhain and P. Nippus, Chem. B. *82,* 408 (1949).

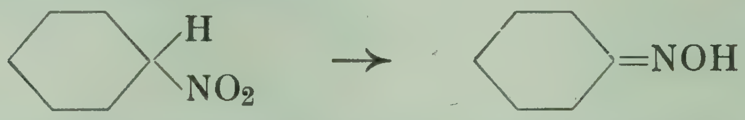
Sulfamic acid *HSO_3NH_2*

516. An intimate mixture of p-nitrobenzamide and sulfamic acid heated to 220° during 20 min., and kept at this temp. for 5 min. → p-nitrobenzonitrile. Y: 94%. F. e. s. A. V. Kirsanov and Y. M. Zolotov, Ж. *20,* 284 (1950); C. A. *44,* 6384i.

Hydroxylaminedisulfonate *$HON(SO_3)_2^{--}$*

Oximes from nitro compounds $CH(NO_2) \rightarrow C{:}NOH$

517.

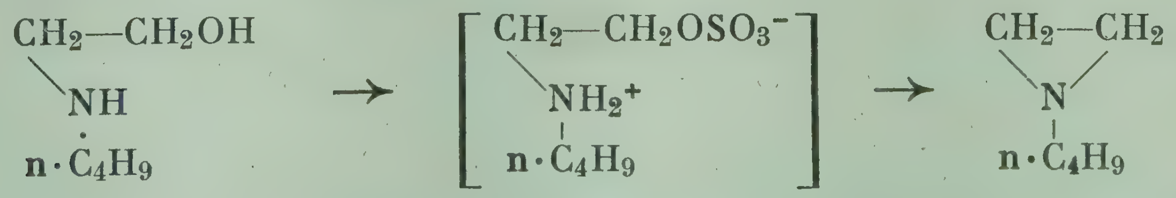


35%-$NaHSO_3$ added slowly to $NaNO_2$ and crushed ice, SO_2 passed in at 0-2° until the soln. is acid to Congo red, the soln. of hydroxylaminedisulfonate thus formed treated with 20%-H_2SO_4 at 4-5°, immediately followed by nitrocyclohexane in a slight excess of aq. NaOH at 6-8°, and stirred 1 hr. → cyclohexanone oxime. Y: 85-90%. S. S. Nametkin, G. I. Zyabreva, and B. A. Krentsel, Doklady Akad. Nauk S. S. S. R. *72,* 711 (1950); C. A. *44,* 9362d.

Chlorosulfonic acid/potassium hydroxide *$ClSO_3H/KOH$*

Cyclic imines from aminoalcohols ○

518.



Chlorosulfonic acid added portionwise with shaking to crude N-(n-butyl)ethanolamine hydrochloride, after the initial reaction has subsided heated 40 min. on a steam bath, then at 80° under water pump vacuum, finally at 140-145° for 1.5 hrs., dissolved in cold water, then added portionwise with vigorous agitation below 70° to aq. KOH, and steam-distilled → N(n-butyl)ethyleneimine. Y: 74%. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. *14*, 605 (1949).

Copper chromite *$CuCr_2O_4$*

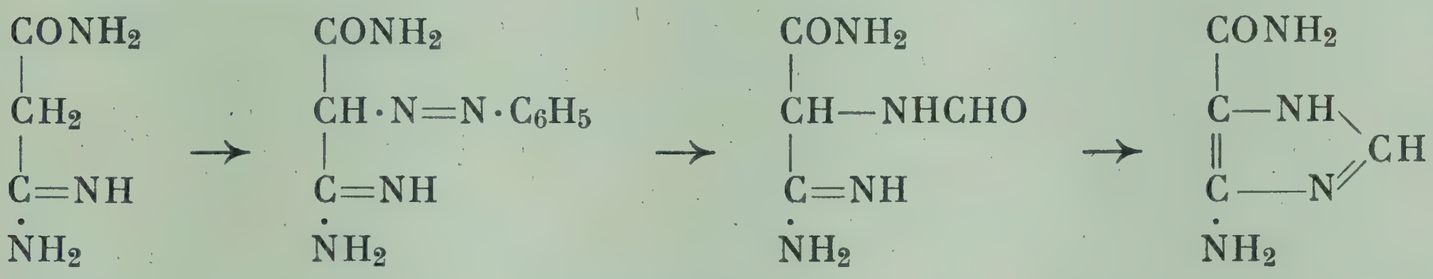
Pyrrolizidines

s. *4*, 390; s. a. Am. Soc. *72*, 2537, 2543 (1950)

Hydrochlorides ←

Imidazoles via azo compounds and formamides

519.

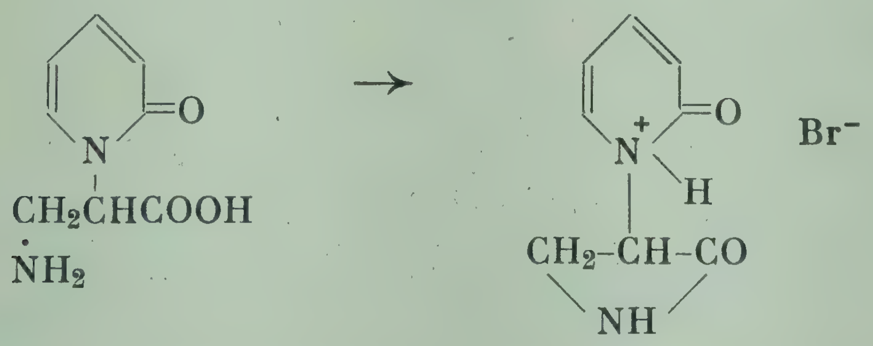


A soln. of aniline in 6 *N* HCl gradually treated below 5° with aq. $NaNO_2$, excess HNO_2 decomposed with urea, the diazonium salt soln. obtained poured into an aq. soln. of malonamamidine hydrochloride, and the pH brought to ca. 4 by addition of concd. aq. Na-acetate → phenylazomalonamamidine hydrochloride (Y: 90%) added in portions with occasional agitation during 1 hr. to a suspension of Zn-dust in 98%-formic acid, and warmed on a hot plate until the residual azo color is discharged → formamidomalonamamidine hydrochloride (Y: 63%) heated ca. 10 min. at an oil-bath temp. of ca. 170° → 4-amino-5-imidazolecarboxamide hydrochloride (Y: 89%). E. Shaw and D. W. Woolley, J. Biol. Chem. *181*, 89 (1949).

Hydrobromic acid *HBr*

β-Lactams

520.

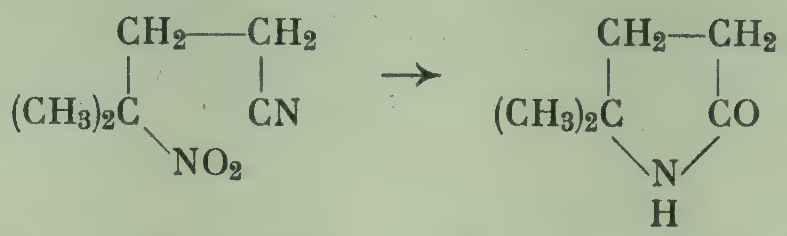


Dry HBr passed into a suspension of α-(N-2-pyridone)-β-aminopropionic acid in abs. ethanol until a clear soln. results, and allowed to stand overnight in a refrigerator → α-(N-2-pyridone)-β-aminopropiolactam hydrobromide. Y: 89%. R. Adams and V. V. Jones, Am. Soc. *71*, 3826 (1949).

Nickel *Ni*

2-Pyrrolidones from nitronitriles

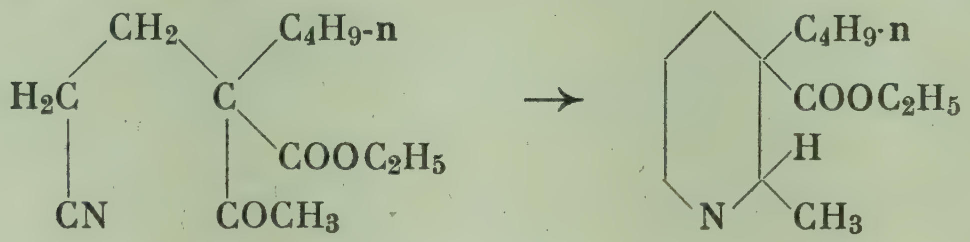
521.



γ-Methyl-γ-nitrovaleronitrile in abs. alcohol hydrogenated with Raney-Ni at 170-240° and an initial pressure of 2200 lbs./sq.in. with final shaking → 2,2-dimethyl-5-pyrrolidone. Y: 58-61%. R. C. Elderfield and H. A. Hageman, J. Org. Chem. *14*, 605 (1949).

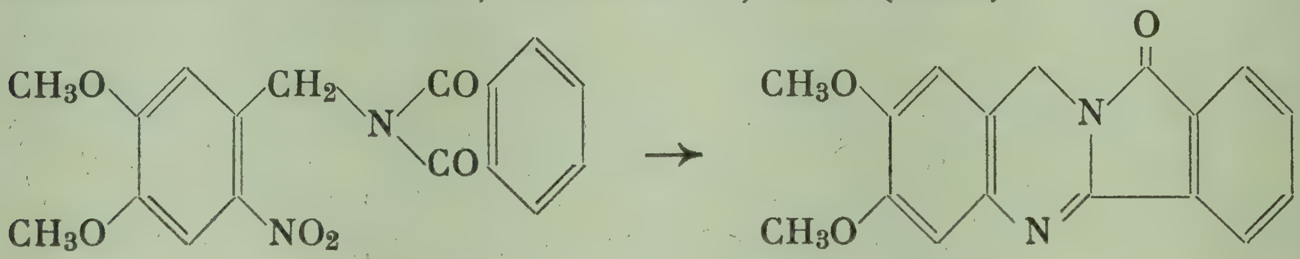
Reductive ring closure

522.



Piperidines. An alc. soln. of ethyl 3-n-butyl-1-cyano-4-pentanone-3-carboxylate hydrogenated 0.5 hr. with 16%Ni-on-fuller's earth at 100° and 80 atm. → ethyl 2-methyl-3-n-butylpiperidine-3-carboxylate. Y: 83%. F. e. s. H. Henecka, Chem. B. *82*, 104 (1949); s. a. N. F. Albertson and J. L. Fillman, Am. Soc. *71*, 2818 (1949); *72*, 2594 (1950); C. F. Koelsch and S. T. Rolfson, Am. Soc. *72*, 1871 (1950).

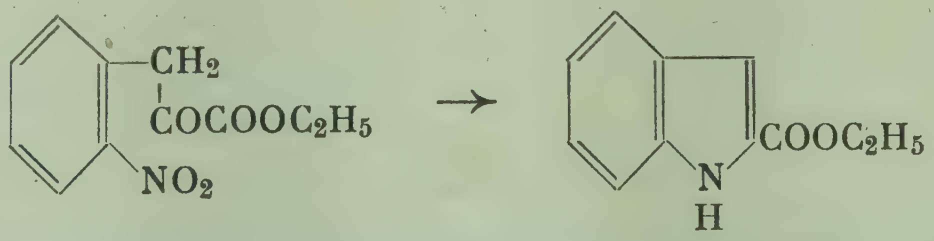
523.



Pyrrolo [2.1-b] quinazoline ring. N-(2-Nitro-4,5-dimethoxybenzyl)phthalimide suspended in hot alcohol and hydrogenated with Raney-Ni at a few hundred mm. pressure → 7,8-dimethoxy-12-keto-10,12-dihydroisoindolo[1.2-b]quinazoline. Y: 75%. F. e. s. A. M. Downes and F. Lions, Am. Soc. *72*, 3053 (1950).

Platinum oxide *PtO₂*

524.



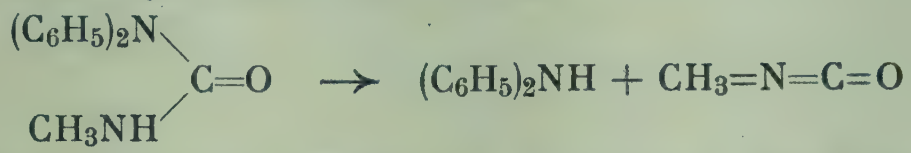
Indoles. A soln. of crude ethyl o-nitrophenylpyruvate in glacial acetic acid hydrogenated with PtO_2 at 3 atm., whereby reduction occurs very rapidly → ethyl indole-2-carboxylate. Y: 80%. W. J. Brehm, Am. Soc. *71*, 3541 (1949).

Nitrogen ↑ NC ⇑ N

Without additional reagents *w.a.r.*

Low molecular isocyanates from ureas ←

525.



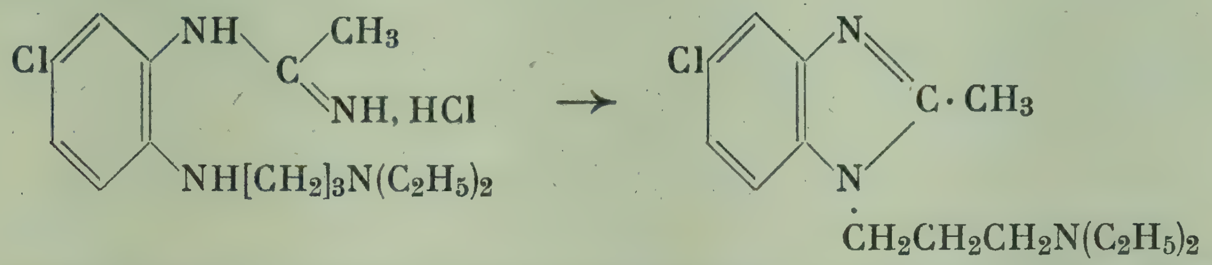
$$\begin{array}{lll}(C_6H_5)_2N\diagdown & & \\ & C{=}O & \longrightarrow (C_6H_5)_2NH + CH_3{=}N{=}C{=}O \\ CH_3NH\diagup & & \end{array}$$

226 gm. N,N-diphenyl-N′-methylurea heated to 240-290° → 57 gm. methylisocyanate and 169 gm. diphenylamine. W. Siefken, A. *562*, 75 (1949).

Acetyl chloride *CH_3COCl*

Benzimidazoles ○

526.

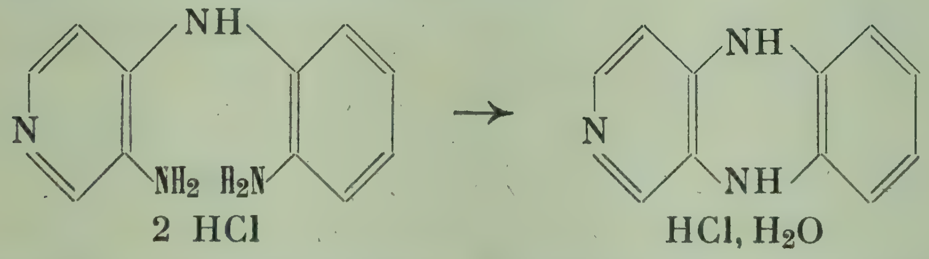


N-[5-Chloro-2-(3-diethylaminopropylamino)phenyl]acetamidine hydrochloride and acetyl chloride refluxed 3 hrs. → 5-chloro-2-methyl-1-(3-diethylaminopropyl)benzimidazole. Y: 92%. F. e. s. F. E. King and R. M. Acheson, Soc. *1949*, 1396.

Hydrochlorides

9,10-Dihydro-2,9,10-triaza-anthracenes ←

527.



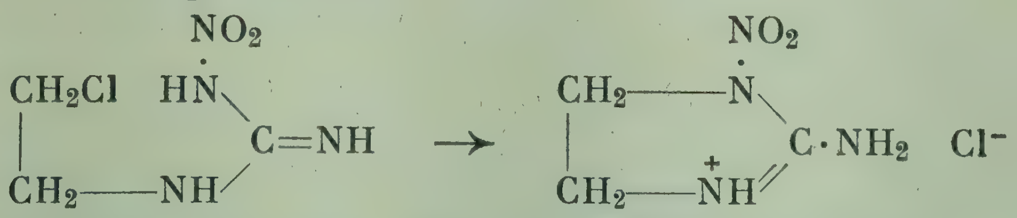
3-Amino-4-o-aminoanilinopyridine dihydrochloride heated 2 min. at its decomposition point (283-284°) → 9,10-dihydro-2,9,10-triaza-anthracene hydrochloride monohydrate. Y: 58%. V. Petrow, J. Saper, and B. Sturgeon, Soc. *1949*, 2540.

Halogen ↑ NC ⇑ Hal

Without additional reagents *w.a.r.*

Imidazolines from guanidines ○

528.



β-Chloroethylnitroguanidine refluxed with 2-pentanol → 1-nitro-2-amino-2-imidazoline hydrochloride. Y: ca. 100%. F. e. s. A. F. McKay and J. E. Milks, Am. Soc. *72*, 1616 (1950).

Pyridine *C_5H_5N*

Isocyanates from carbamyl chlorides NHCOCl → N:C:O

s. *6*, 455

Sulfur ↑ NC ⇑ S

Sodium hydroxide *NaOH*

Guanidines from sulfonylguanidines ←

s. *4*, 465; s. a. R. *68*, 595 (1949)

Lead acetate *$(CH_3COO)_2Pb$*

Cyanamides from thioureas $NHCSNH_2$ → NHCN

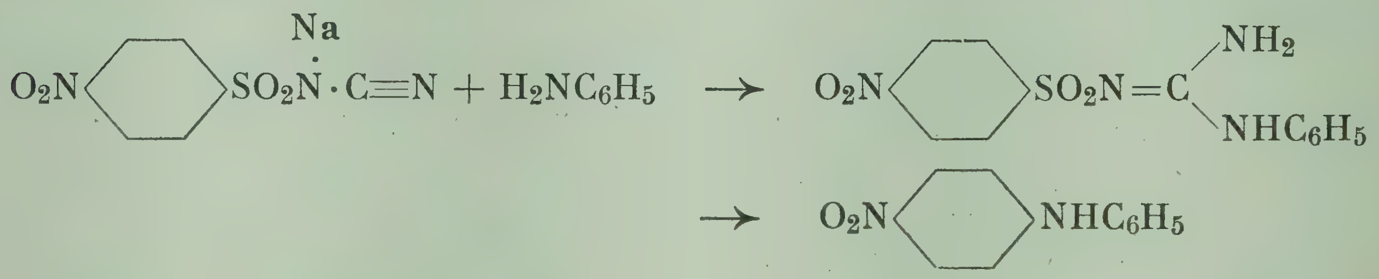
s. *4*, 466; s. a. F. Kurzer, Org. Synth. *31*, 19 (1951)

Carbon ↑ NC ⇑ C

Sodium hydroxide *NaOH*

Sec. from prim. amines and N-sulfonylcyanamides via sulfonylguanidines ←

529.

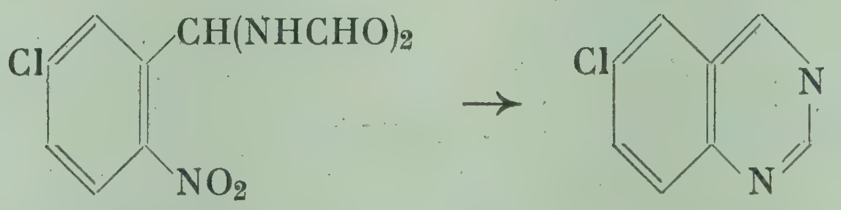


Na salt of p-nitrophenylsulfonylcyanamide and aniline dissolved in glacial acetic acid and boiled 10 min. → N-p-nitrophenylsulfonyl-N′-phenylguanidine (Y: 78%) boiled several min. with 2 *N* NaOH → 4-nitrodiphenylamine (Y: 97%). F. e. s. H. J. Backer et al., R. *68*, 595 (1949); *69*, 1348 (1950).

Zinc *Zn*

Quinazolines ○

530.



5-Chloro-2-nitrobenzylidenebisformamide and Zn-dust treated with acetic acid and crushed ice during 10 min., shaken for 0.5 hr., then stirred with addition of small amounts of Zn for 1.5 hrs. → 6-chloroquinazoline. Y: 84%. F. e. s. K. Schofield and T. Swain, Soc. *1949*, 1367.

Acetic anhydride $(CH_3CO)_2O$

Nitriles from α-oximinocarboxylic acids $C(:NOH)COOH \rightarrow CN$

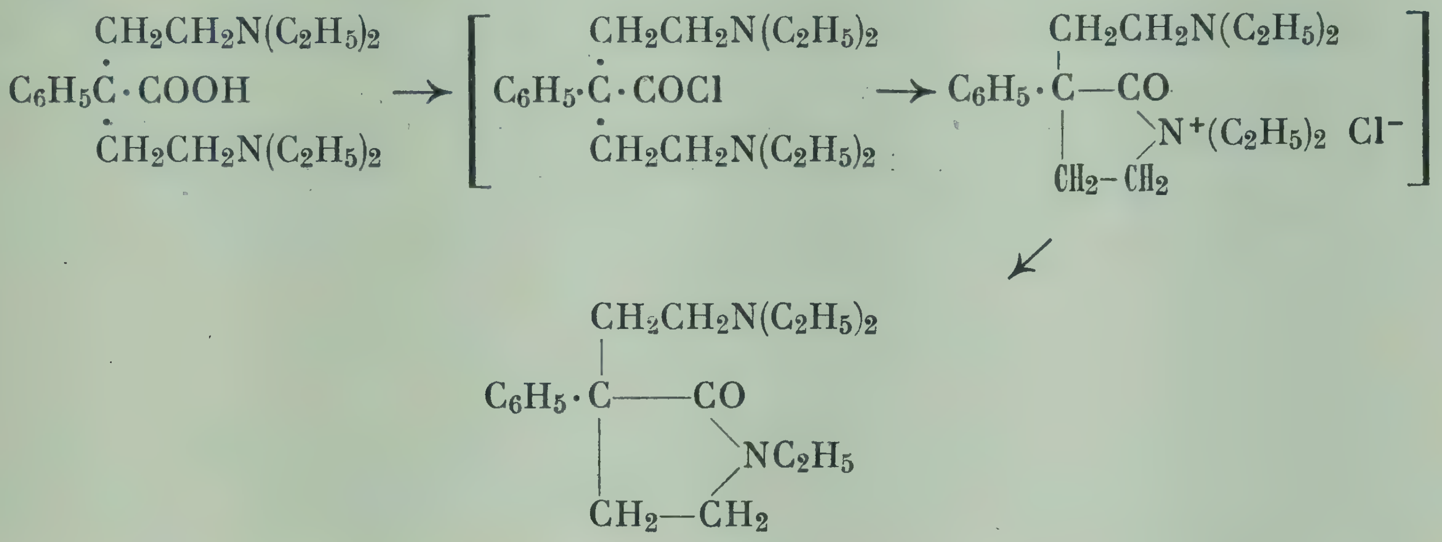
s. *6,* 823

Thionyl chloride $SOCl_2$

Lactams ○

s. *5,* 374; s. a. A. L. Morrison, M. Königstein, and A. Cohen, Soc. *1950,* 2887

531.



N-subst. 2-Pyrrolidones and 2-piperidines. An intramolecular reaction between acid chlorides and tert. amines, with the simultaneous elimination of alkyl halides can be applied to the synthesis of pyrrolidones and piperidones.—E: α,α-Bis-(β-diethylaminoethyl)phenylacetic acid added slowly with vigorous stirring at 5-10° to $SOCl_2$, warmed, whereby acid chloride-formation occurs between 25 and 60° and ethyl chloride evolution between 70 and 80°, finally refluxed at 85-88° for 1.5 hrs. → 1-ethyl-3-(β-diethylaminoethyl)-3-phenyl-2-pyrrolidone. Y: 70%.—This reaction can also be used for the opening of N-hetero rings. F. e. s. R. L. Clarke et al., Am. Soc. *71,* 2821 (1949).

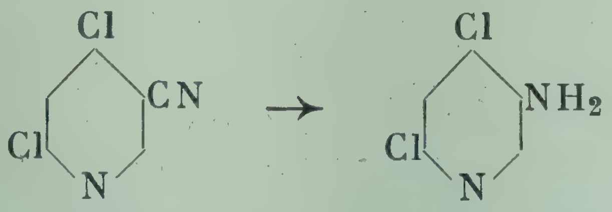
Alkali hypohalites ←

Hofmann degradation $CONH_2 \rightarrow NH_2$

s. *2,* 464, 475/6; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, Am. Soc. *72,* 3539 (1950)

Amines from nitriles $CN \rightarrow NH_2$

532.



2,4-Dichloropyridine-5-carbonitrile (prepn. s. 429) shaken with a soln. of Br in 7%-KOH at room temp. for a few hrs., then warmed on a water bath at 70° for a few more hrs. → 5-amino-2,4-dichloropyridine. Y: 30-40%. H. J. den Hertog et al., R. *69,* 673 (1950).

Formation of Hal—Hal Bond

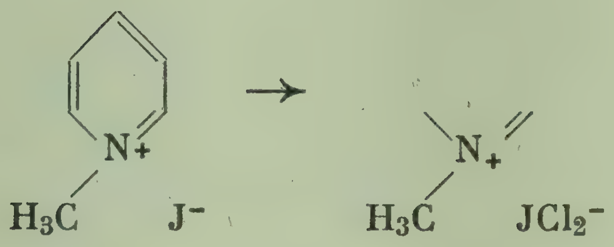
Exchange

Halogen ↑ **HalHal ⇅ Hal**

Thionyl chloride *$SOCl_2$*

Chloroiodates ←

533.



$SOCl_2$ added to dry methylpyridinium iodide → methylpyridinium chloroiodate. Y: 73%. F. e. s. W. B. Brownell and L. C. King, Am. Soc. *71*, 2926 (1949).

Formation of Hal—S Bond

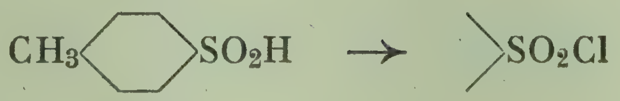
Exchange

Hydrogen ↑ **HalS ⇅ H**

Cupric chloride *$CuCl_2$*

Sulfonic acid chlorides from sulfinic acids $SO_2H \rightarrow SO_2Cl$

534.



A soln. of Na-p-toluenesulfinate in HCOOH added to a soln. of $CuCl_2$ in HCOOH-water → p-toluenesulfonyl chloride. Y: ca. 100%. E. Pfeil and O. Velten, A. *565*, 183 (1949).

Chlorine *Cl*

Sulfonic acid chlorides from mercaptans $SH \rightarrow SO_2Cl$

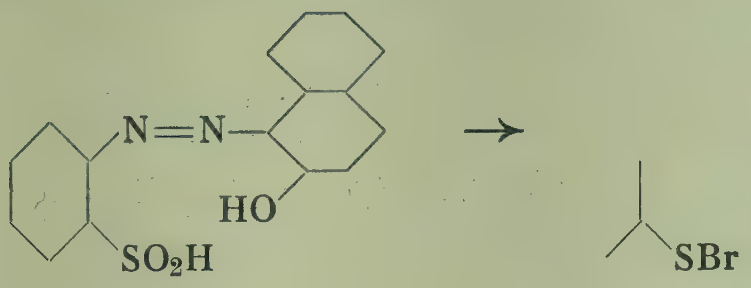
s. *3*, 418; s. a. R. O. Roblin, Jr., and J. W. Clapp, Am. Soc. *72*, 4890 (1950)

Oxygen ⇅ HalS ⇅ O

Acetic acid *CH_3COOH*

Sulfenyl bromides from sulfinic acids $SO_2H \rightarrow SBr$

535.



A suspension of o-(2-hydroxy-1-naphthylazo)benzenesulfinic acid in glacial acetic acid containing 48%-HBr shaken for 48 hrs. at room temp. → o-(2-hydroxy-1-naphthylazo)phenylsulfenyl bromide (startg. m. f. 644). Y: ca. 100%. A. Burawoy and C. Turner, Soc. *1950*, 469.

Thionyl chloride *$SOCl_2$*

Sulfonic acid chlorides from sulfonic acids $SO_3H \rightarrow SO_2Cl$

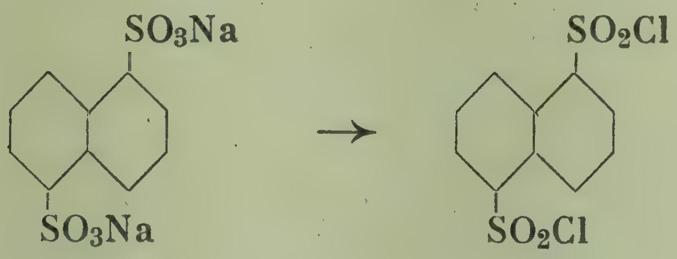
536. $CH_3SO_3H \rightarrow CH_3SO_2Cl$

$SOCl_2$ added at 95° to methanesulfonic acid over a period of 4 hrs., and heating continued at the same temp. for 3.5 hrs. → methanesulfonyl chloride. Y: 71-83%. P. J. Hearst and C. R. Noller, Org. Synth. *30*, 58 (1950).

Chlorosulfonic acid *$ClSO_3H$*

Sulfonic acid chlorides from sodium sulfonates $SO_3Na \rightarrow SO_2Cl$

537.



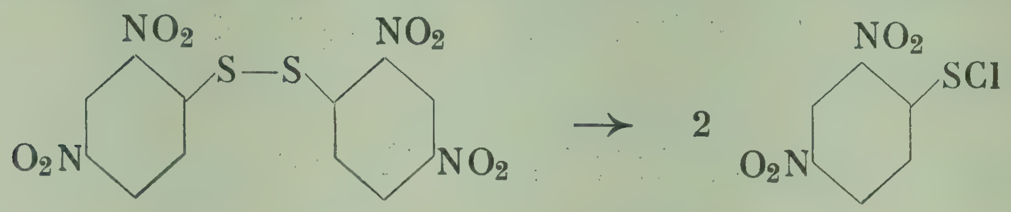
Dry di-Na-1,5-naphthalenedisulfonate heated 2 hrs. with chlorosulfonic acid at 98° → naphthalene-1,5-disulfonyl dichloride. Y: 93.7%.—At higher temp., the yield declines sharply. F. reaction conditions s. A. A. Spryskov and N. V. Apar'eva, Ж. *19*, 1576 (1949); *20*, 1818 (1950); C. A. *44*, 1082i; *45*, 2434a; s. a. B. A. Everard and J. A. Mills, Soc. *1950*, 3386.

Sulfur ↑ **HalS ⇅ S**

Fuming sulfuric acid H_2SO_4,SO_3

Sulfenylhalides from disulfides RSSR → 2 RSCl

538.



Cl_2 introduced into a suspension of 2,4-dinitrophenyl disulfide in ethylene chloride in the presence of 3 drops of fuming H_2SO_4 at an initial temp. of ca. 25° for 30-35 min. → 2,4-dinitrobenzenesulfenyl chloride. Y: ca. 86%. F. e., catalysts, and inhibitors s. N. Kharasch, G. J. Gleason, and C. M. Buess, Am. Soc. *72*, 1796 (1950).

Formation of Hal—Rem Bond

Uptake

Addition to Remaining Elements HalRem ⇓ Rem

Without additional reagents *w.a.r.*

Selenium dibromides from selenides $R_2Se \rightarrow R_2SeBr_2$

539. $(p\text{-}CH_3OC_6H_4)_2Se \rightarrow (p\text{-}CH_3OC_6H_4)_2SeBr_2$

A soln. of Br_2 in CS_2 added quickly to a soln. of di-p-methoxyphenyl selenide in the same solvent → di-p-methoxyphenyl selenium dibromide. Y: ca. 100%. G. V. Boyd, M. Doughty, and J. Kenyon, Soc. *1949*, 2196.

Exchange

Hydrogen ↑ HalRem ⇅ H

Without additional reagents *w.a.r.*

Halogenosilanes from silanes SiH → SiHal

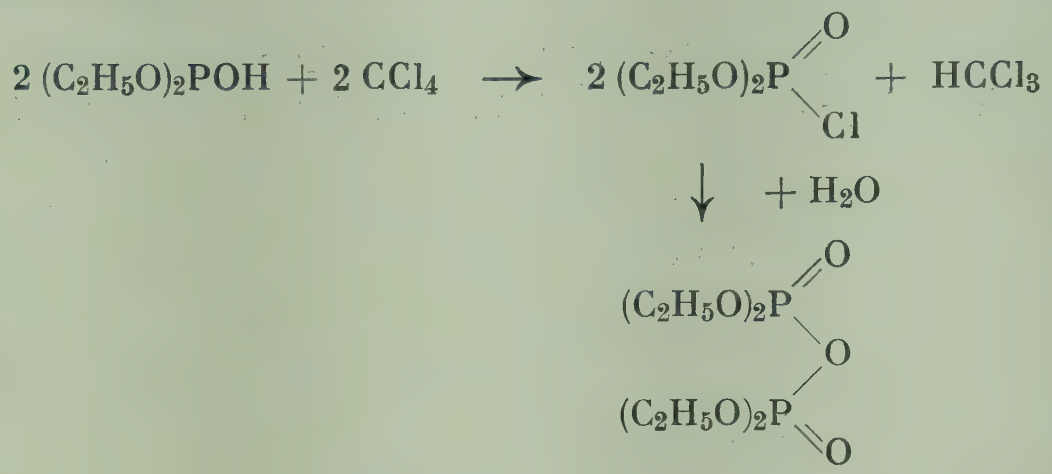
540. $(C_2H_5)_2SiH \rightarrow (C_2H_5)_3SiJ$

Triethylsilane added dropwise during ¼ hr. to iodine, then refluxed 0.5 hr. in a dry N_2-stream to carry off HI while more triethylsilane is added to remove the remaining iodine, a little Mg-powder added, and fractionated → triethyliodosilane. Y: 85%. C. Eaborn, Soc. *1949*, 2755; also bromosilanes s. W. H. Nebergall and O. H. Johnson, Am. Soc. *71*, 4022 (1949); *72*, 4702 (1950); chlorosilanes s. J. W. Jenkins and H. W. Post, J. Org. Chem. *15*, 552 (1950).

Triethylamine/polyhalogenalkane ←

Chlorophosphoric acid esters and pyrophosphoric acid esters from dialkylphosphites ←

541.



Triethylamine added slowly at 0° to a stirred mixture of diethyl phosphite and CCl_4, the temp. maintained at 0° for 15 min., then allowed to rise to room temp., and stirred for 3 hrs. → diethyl chlorophosphate. Y: 81%.—In the presence of water, tetraethyl pyrophosphate (Y: 73%) is formed. F. e. s. G. M. Steinberg, J. Org. Chem. *15*, 637 (1950).

Oxygen ↑ HalRem ↑↓ O

Sulfur dioxide/iodine SO_2/I

Dichloroarsines from arsonic acids $AsO_3H_2 \rightarrow AsCl_2$

542. $C_6H_5AsO_3H_2 \rightarrow C_6H_5AsCl_2$

A little iodine added to a soln. of phenylarsonic acid in concd. HCl, then SO_2 passed in with efficient stirring below 50° for 1.75 hrs. → phenyldichloroarsine (startg. m. f. 676). Crude Y: 91%. R. L. Barker et al., J. Soc. Chem. Ind. *68*, 289 (1949).

Halogen ↑ HalRem ↑↓ Hal

Aluminum iodide AlI_3

Siloxanes from fluorosilanes via iodosilanes ←

543. $2\,(n\text{-}C_3H_7)_3SiF \rightarrow 2\,(n\text{-}C_3H_7)_3SiJ \rightarrow (n\text{-}C_3H_7)_3Si\cdot O\cdot Si(n\text{-}C_3H_7)_3$

Tri-n-propylfluorosilane boiled with AlI_3 for 0.5 hr. → tri-n-propyliodosilane (Y: 70%) shaken several times with water, dried, and distilled → hexa-n-propyldisiloxane (Y: 76%). F. e. s. C. Eaborn, Soc. *1949*, 2755.

Sulfur ↑ HalRem ⇅ S

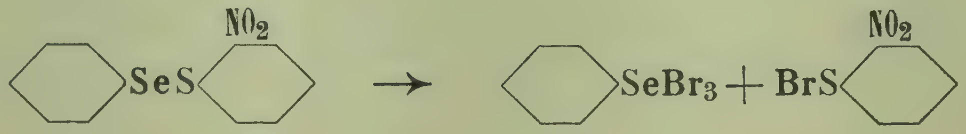
Without additional reagents *w.a.r.*

Chlorothiophosphoric acid esters from dithiophosphoric acids $(RO)_2PSSH \rightarrow (RO)_2PSCl$

s. *6*, 156

Selenyltribromides and sulfenylbromides from selenylsulfides ←

544.



Br_2 added dropwise with ice-water cooling and shaking to a soln. of phenylselenyl o-nitrophenyl sulfide in chloroform, and worked up after 2 hrs. at room temp. → phenyl selenyltribromide (Y: 96.1%) and o-nitrophenyl sulfenylbromide (Y: 98.3%). H. Rheinboldt and E. Giesbrecht, A. *568*, 198 (1950).

Carbon ↑ HalRem ⇅ C

Without additional reagents *w.a.r.*

Halogeno-lead compounds, organo ←

545. $(C_6H_5)_4Pb + HCl \rightarrow (C_6H_5)_3PbCl$

A stream of dry HCl passed into a boiling soln. of tetraphenyl-Pb in chloroform for 55 min. → triphenyl-Pb chloride (startg. m. f. 674). Y: 75%. H. Gilman and D. S. Melstrom, Am. Soc. *72*, 2953 (1950); s. a. R. Heap and B. C. Saunders, Soc. *1949*, 2983.

Aluminum iodide *AlI_3*

Iodosilanes from silanes ←

546. $(C_2H_5)_4Si \rightarrow (C_2H_5)_3SiJ + JC_2H_5$

Tetraethylsilane refluxed ¾ hr. in the presence of AlI_3 while iodine is added repeatedly → triethyliodosilane (Y: 77%) and ethyl iodide (Y: 90%). F. e. s. C. Eaborn, Soc. *1949*, 2755.

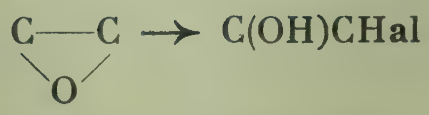
Formation of Hal—C Bond

Uptake

Addition to Oxygen and Carbon HalC ⇓ OC

Without additional reagents *w.a.r.*

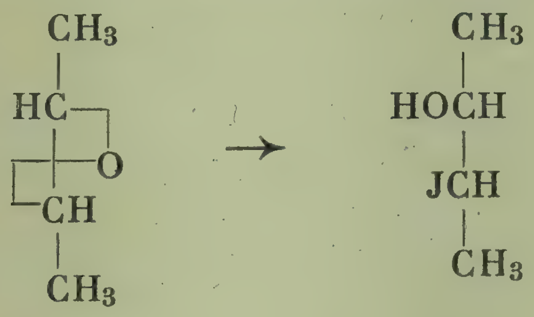
Halogenhydrins from oxido compounds



$C—C \rightarrow C(OH)CHal$ (with O bridging the two C atoms)

s. *4*, 475; s. a. O. E. van Lohuizen and H. J. Baker, R. *68*, 1137 (1949); steroids s. D. H. R. Barton and E. Miller, Am. Soc. *72*, 370, 1066 (1950)

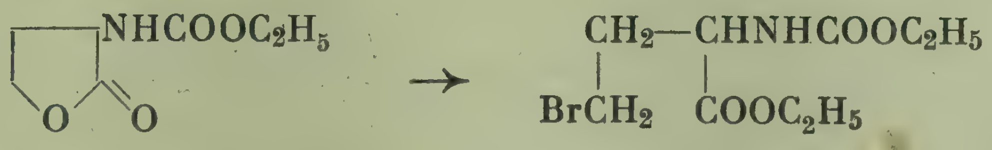
547.



Walden inversion. 55%-aq.-HI added dropwise with vigorous stirring at —10 to 0° to D(+)-2,3-epoxybutane over a period of ca. 40 min., and stirring continued for ca. 10 Min. → L(+)-*erythro*-3-iodo-2-butanol. Y: 75%.—A single Walden inversion accompanies the opening of the ring. F. e. s. H. J. Lucas and H. K. Garner, Am. Soc. *72*, 2145 (1950).

Halogenocarboxylic acid esters from lactones C

548.



Carbethoxyaminobutyrolactone dissolved at 0° in satd. alc. HBr, and allowed to stand below 10° for 24 hrs. → ethyl γ-bromo-α-carbethoxyaminobutyrate. Y: 80%. H. Plieninger, B. *83*, 268 (1950).

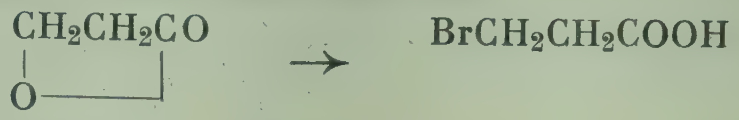
Potassium iodide/phosphoric acid *KI/H_3PO_4*

s. Phosphoric acid/potassium iodide

Magnesium bromide *$MgBr_2$*

Halogenocarboxylic acids from lactones

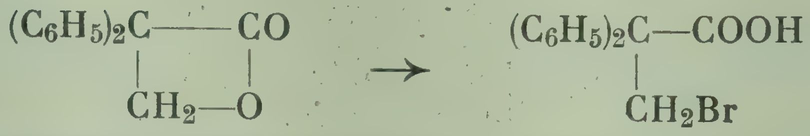
549.



β-Propiolactone added to $MgBr_2$-dietherate in anhydrous ether → β-bromopropionic acid. Y: 83%. T. L. Gresham et al., Am. Soc. *71*, 2807 (1949).

Acetic acid *CH_3COOH*

550.



α,α-Diphenyl-β-propiolactone added to glacial acetic acid (satd. with dry HBr), and allowed to stand 20 hrs. at room temp. → 2,2-diphenyl-3-bromopropanoic acid. Y: 93% F. e. s. H. E. Zaugg, Am. Soc. *72*, 2998 (1950).

Phosphorus *P*

α,γ-Dibromocarboxylic acid bromides from γ-lactones

s. *6*, 569

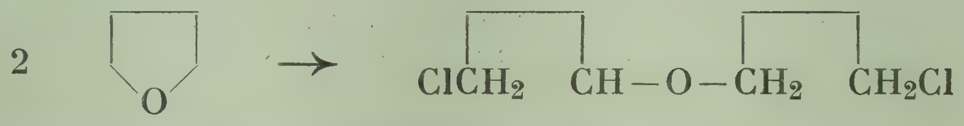
Phosphoric acid/potassium iodide *H_3PO_4/KI*

Tetrahydrofuran ring opening

s. *6*, 584

Phosphorus oxychloride/sulfuric acid *$POCl_3/H_2SO_4$*

551.



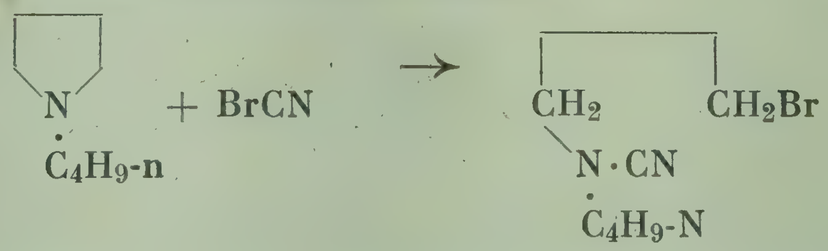
$POCl_3$ followed by concd. H_2SO_4 added with cooling to dry tetrahydrofuran, and the reaction allowed to proceed at 90-100° → 4,4′-dichlorodibutyl ether. Y: 52-54%. K. Alexander and H. V. Towles, Org. Synth. *30*, 27 (1950).

Addition to Nitrogen and Carbon HalC ⇓ NC

Without additional reagents *w.a.r.*

Halogenocyanamides from cyclic imines C

552.



1-n-Butylpyrrolidine in dry benzene added with stirring during 2.5 hrs. to a soln. of cyanogen bromide in dry benzene, and allowed to stand overnight → n-butyl-δ-bromobutylcyanamide. Y: ca. 100%. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. *14*, 605 (1949).

Addition to Carbon HalC ⇓ CC

Without additional reagents *w.a.r.*

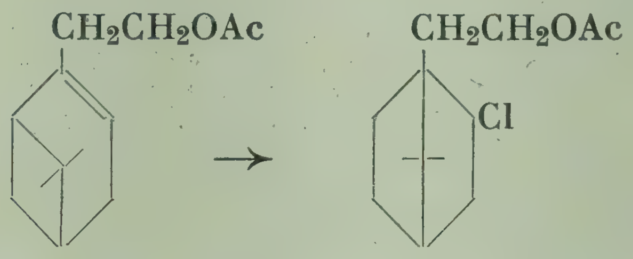
Halides from ethylene derivatives C:C → CHCHal

553. $C_6H_5COCH{=}CHCOOH \rightarrow C_6H_5COCH_2CHBrCOOH$

A vigorous stream of HBr passed for 20 min. into a soln. of β-benzoylacrylic acid in glacial acetic acid with ice cooling, then allowed to stand at room temp. for 3 hrs. → α-bromo-β-benzoylpropionic acid. Y: 90%.—Similarly: α-Chloro-β-benzoylpropionic acid. Y: 81%. E. Buchta and S. Danner, Chem. B. *82*, 63 (1949).

Chlorides from ethylene derivatives with rearrangement ←

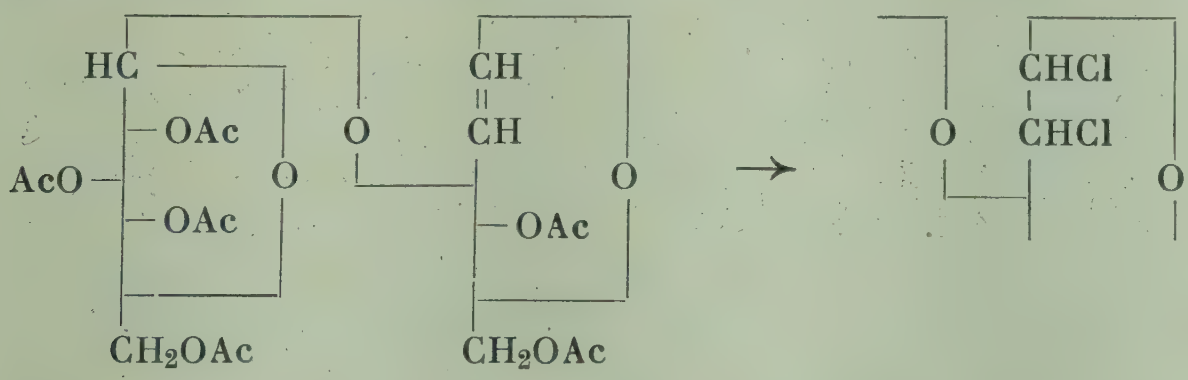
554.



HCl passed at 2-10° into a soln. of nopyl acetate in ethylene chloride until absorption is complete, and allowed to warm to room temp. overnight → 2-chloro-1-apocamphane-β-ethyl acetate. Y: 70-75%. J. P. Bain et al., Am. Soc. *72*, 3124 (1950).

1,2-Dihalides from ethylene derivatives C:C → CHalCHal

555.



A dry stream of chlorine introduced with cooling into a soln. of hexaacetylglucosido-3-glucal in dry chloroform until a test with bromine water indicates the end of the reaction → 1,2-dichlorohexaacetylglucosido-3-glucose. Y: 79%. Similarly: Dibromo derivative. Y: 73%. A. M. Gakhokidze, Ж. *19*, 2082 (1949); C. A. *44*, 3914b; chlorination s. a. M. Jacobson, Am. Soc. *72*, 1489 (1950).

s. a. *6*, 575

Protection of a double bond
s. *6,* 280

Light

556. $$CH_3CH{=}CHCOOH \rightarrow CH_3CHBrCHBrCOOH$$

1,2-Dibromides. Crotonic acid in CCl_4 treated with Br_2 below 60° with illumination over a period of 4.5 hrs. → *α,β*-dibromobutyric acid. Y: 90%.—Illumination allows working at lower temp. Substitution can thus be avoided. F. e. s. P. Seifert et al., Helv. *33,* 725 (1950); *α,β*-dibromonitro compounds s. W. K. Noyce, C. H. Coleman, and J. T. Barr, Am. Soc. *73,* 1295 (1951).

Potassium iodide/phosphoric acid *KI/H_3PO_4*

s. Phosphoric acid/potassium iodide

Calcium hypochlorite *$Ca(OCl)_2$*

Chlorohydrins from ethylene derivatives
$C{:}C \rightarrow C(OH)CCl$

557. CO_2 bubbled into a stirred cooled mixture of diallyl ether, water, and $Ca(OCl)_2$ until after ca. 4 hrs. titration indicates that the reaction is complete → diallyl ether di(chlorohydrin). Crude Y: 94.4%. H. Wittcoff, J. R. Roach, and S. E. Miller, Am. Soc. *71,* 2666 (1949).

Stannic chloride *$SnCl_4$*

Chlorides from ethylene derivatives
$C{:}C \rightarrow CHCCl$

s. *5,* 389; s. a. Bl. *1949,* 396

Nitrosyl chloride *NOCl*

Reaction of nitrosyl chloride with ethylene derivatives ←
1,2-Nitrohalides and 1,2-dihalides

558.

$$\begin{tikzcd}
 & O_2NCH_2CHClCH_2Cl \\
CH_2{=}CHCH_2Cl \arrow[ur] \arrow[dr] & \\
 & ClCH_2CHClCH_2Cl
\end{tikzcd}$$

24 gm. allyl chloride in 3 equal portions allowed to stand in a sealed tube with NOCl at room temp. for 12-24 hrs. until the red color disappears → 18.4 gm. 1,2-dichloro-3-nitropropane, 4 gm. 1,2,3-trichloropropane, and 9 gm. starting material. F. e. s. A. Y. Yakubovich and A. L. Lemke, Ж. *19,* 649 (1949); C. A. *44,* 1011b.

Phosphoric acid/potassium iodide *H_3PO_4/KI*

Iodides from ethylene derivatives C:C → CHCl
s. *6*, 584

Hypochlorite *ClO^-*

Chlorohydrins from ethylene derivatives C:C → C(OH)CCl

with NaOCl s. *4*, 484; s. a. M. Naudet, Bl. *1950*, 842; with $Ca(OCl)_2$ s. *6*, 557

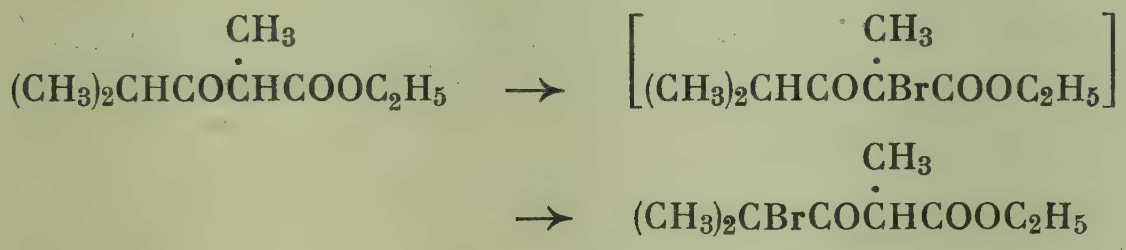
Rearrangement

Hydrogen/Carbon Type HalC ↶ HC

Hydrobromic acid *HBr*

Bromination with migration of bromine ←

559.



$$(CH_3)_2CHCO\overset{CH_3}{C}HCOOC_2H_5 \rightarrow \left[(CH_3)_2CHCO\overset{CH_3}{C}BrCOOC_2H_5\right] \rightarrow (CH_3)_2CBrCO\overset{CH_3}{C}HCOOC_2H_5$$

Br_2 in CCl_4 added dropwise below 5° to a rapidly stirred soln. of ethyl α-isobutyrylpropionate in CCl_4, and allowed to stand in the cold-room to complete the rearrangement to the γ-bromoester → ethyl γ-bromo-α-isobutyrylpropionate. Y: 95%. E. B. Reid, R. B. Fortenbaugh, and H. R. Patterson, J. Org. Chem. *15*, 572 (1950); *16*, 33 (1951); s. a. A. Becker, Helv. *32*, 1584 (1949).

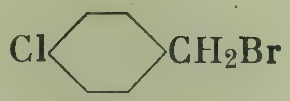
Exchange

Hydrogen ↑ HalC ⇅ H

Without additional reagents *w.a.r.*

Bromination H → Br

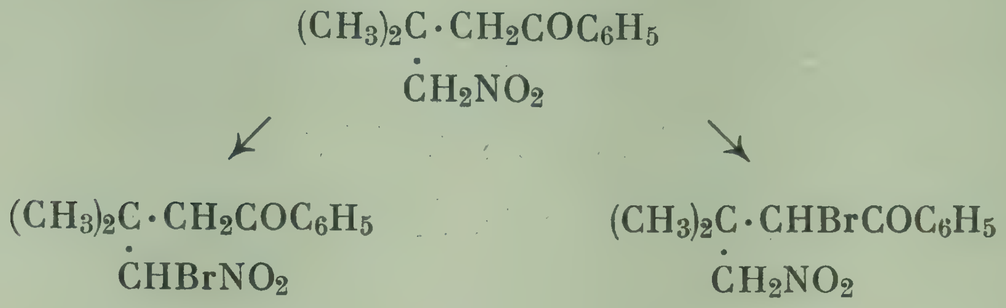
560.



Br_2 added in portions during ca. ¾ hr. to p-chlorotoluene at 140-150° in a pressure bottle, which is opened at each addition of Br_2, finally heated at 140-150° for an additional 0.5 hr. → p-chlorobenzyl bromide. Y: 89%. F. Kröhnke, Chem. B. *83*, 35 (1950).

Aliphat. nitrohalides from aliphat. nitro compounds

561.



$$(CH_3)_2\underset{CH_2NO_2}{C}\cdot CH_2COC_6H_5 \;\to\; (CH_3)_2\underset{CHBrNO_2}{C}\cdot CH_2COC_6H_5 \quad\text{and}\quad (CH_3)_2\underset{CH_2NO_2}{C}\cdot CHBrCOC_6H_5$$

β,β-Dimethyl-γ-nitrobutyrophenone

treated slowly below 5^0 with a soln. of Na in dry methanol, after 15 min. the soln. of the *aci*-nitro compound so obtained added dropwise with stirring at 0^0 to a soln. of Br_2 in dry chloroform, cooling discontinued, and stirred 35 min. more → β,β-dimethyl-γ-bromo-γ-nitrobutyrophenone startg. m. f. 881. Crude Y: 92.5%.

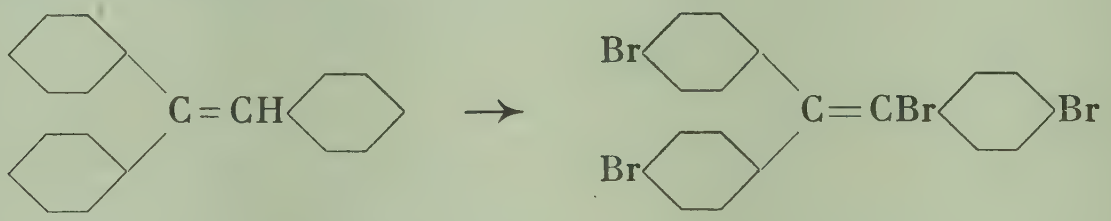
dissolved in dry chloroform, treated dropwise with liq. Br_2 over a period of 45 min., then stirred for 1 hr. → β,β-dimethyl-α-bromo-γ-nitrobutyrophenone. Y: 96%.

F. e. for the γ-bromination in alkaline medium s. L. I. Smith and V. A. Engelhardt, Am. Soc. *71*, 2671, 2676 (1949).

Reaction of bromine vapor with solid compounds

α,β-Ethylenebromides from ethylene derivatives

562.



When solid aryl olefins are treated with bromine vapor, p-positions of unsubst. phenyl groups are brominated. Highly subst. double bonds do not add bromine but undergo substitution of bromine for hydrogen. —E: Triphenylethylene treated 17 hrs. with bromine vapor → bromotri-(p-bromophenyl)ethylene. Y: 77%. F. e. s. R. E. Buckles, E. A. Hausman, and N. G. Wheeler, Am. Soc. *72*, 2494 (1950); bromination in p-position s. a. Org. Synth. *31*, 29 (1951).

Bromination with migration of bromine

s. *6*, 559

Sodium acetate *CH_3COONa*

Bromination

s. *3*, 155; *4*, 489; α-bromoketones s. V. R. Mattox and E. C. Kendall, J. Biol. Chem. *188*, 287 (1951)

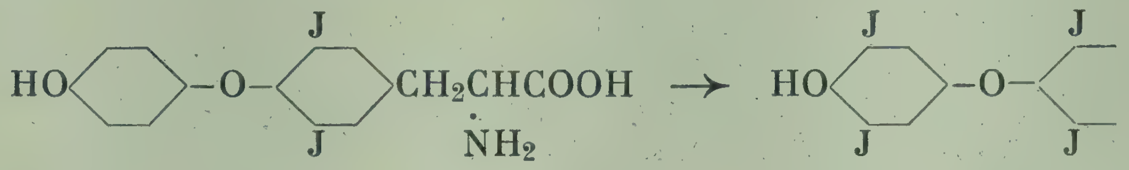
Sodium acetate/phosphoric acid *CH_3COONa/H_3PO_4*

s. Phosphoric acid/sodium acetate

Ethylamine/potassium iodide *$C_2H_5NH_2/KI$*

Iodination H → I

563.

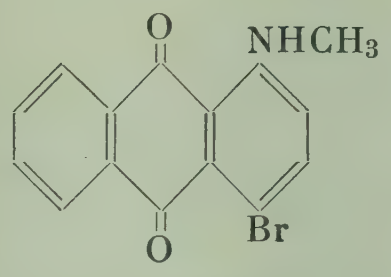


A soln. of iodine in KI-soln. added dropwise to a stirred soln. of 3,5-diiodothyronine in aq. ethylamine soln., and stirring continued for 10 min. → thyroxine. Y: 90%.—The use of aq. or alc. prim. or sec. aliphatic amine soln. is preferable to the use of aq. NH_3, which may form explosive nitrogen iodides. J. C. Clayton and B. A. Hems, Soc. *1950*, 840; cf. Soc. *1950*, 2824; J. A. Goodson et al., Brit. J. Pharmacol. *3*, 49 (1948); with NaOH s. D. Papa et al., Am. Soc. *72*, 2619, 4906 (1950).

Pyridine *C_5H_5N*

Bromination H → Br

564.

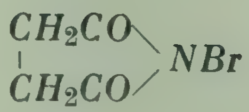


Br_2 added with stirring to 1-methylaminoanthraquinone (prepn. s. 491) and pyridine over a period of 9-10 min., then heated on a steam bath for 6 hrs. → 1-methylamino-4-bromoanthraquinone. Y: 70-74%. C. V. Wilson, Org. Synth. *29*, 68 (1949).

s. a. *5*, 395; R. Kuhn and K. Dury, A. *571*, 44 (1951)

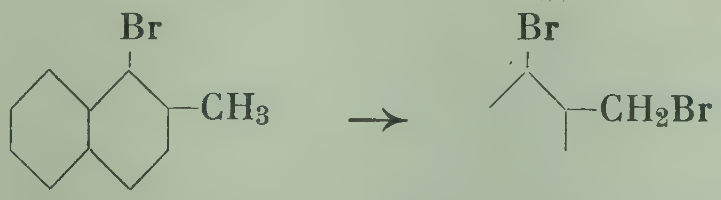
N-Bromosuccinimide

Bromination



$\begin{matrix}CH_2CO\\ |\\ CH_2CO\end{matrix}\!>\!NBr$

565.

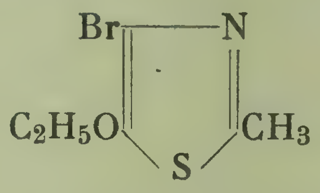


A mixture of 1-bromo-2-methylnaphthalene, N-bromosuccinimide, a little benzoylperoxide, and CCl_4 refluxed 2.5 hrs. → 1-bromo-2-bromomethylnaphthalene. Y: 85%.—High temp. bromination at 230-240° gave yields which never exceeded 59%. W. S. Newman and A. I. Kosak, J. Org. Chem. *14*, 375 (1949); s. a. A. C. Cope and S. W. Fenton, Am. Soc. *73*, 1668, 1673 (1951).

s. a. *6*, 840

N-Bromosuccinimide/benzoyl peroxide

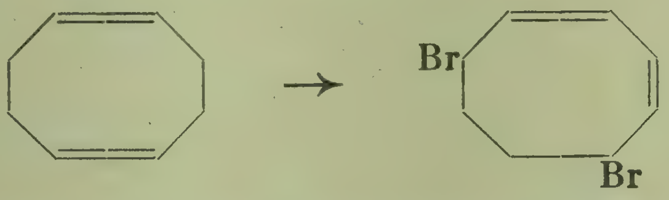
566.



Isosters. N-Bromosuccinimide and benzoyl peroxide added to 2-methyl-5-ethoxythiazole (prepn. s. 638) in dry CCl_4, and refluxed 1 hr. after the spontaneous reaction has subsided → 2-methyl-4-bromo-5-ethoxythiazole. Y: 81%.—The 5-ethoxyl group promotes electrophilic attack in the 4-position, just as the 3-ethoxyl group of the isosteric pyridine favors electrophilic attack in the 2-position of the pyridine ring. D. S. Tarbell, H. P. Hirschler, and R. B. Carlin, Am. Soc. *72*, 3138 (1950).

Bromination of unsatd. compounds in the allyl position with rearrangement ←

567.

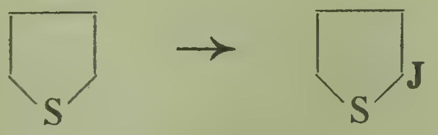


A mixture of 1,5-cyclooöctadiene, N-bromosuccinimide, benzoyl peroxide, and CCl_4 refluxed 3 hrs. with stirring → 5,8-dibromo-1,3-cyclooöctadiene. Y: 86%. A. C. Cope, C. L. Stevens, and F. A. Hochstein, Am. Soc. *72*, 2510 (1950).

Nitric acid *HNO_3*

Iodination H → I

568.



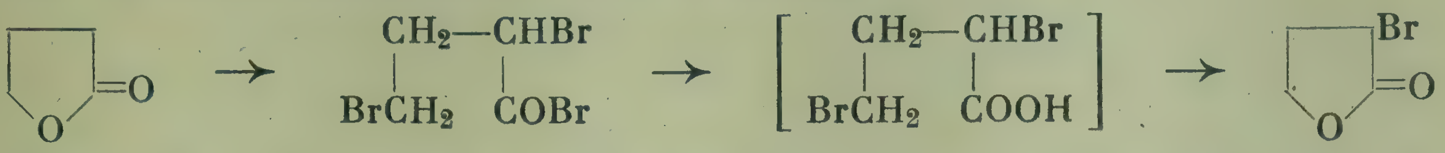
HNO_3 added slowly with vigorous stirring to thiophene and iodine, with slight heating to start the reaction and occasional cooling to control it, then refluxed on a water bath for 30 min. after all the HNO_3 has been added → 2-iodothiophene. Y: 68-72%. H. Y. Lew and C. R. Noller, Org. Synth. *30*, 53 (1950); Am. Soc. *72*, 5715 (1950).

Phosphorus *P*

α-Bromo-γ-lactones from γ-lactones via α,β-dibromocarboxylic acid bromides

H → Br

569.

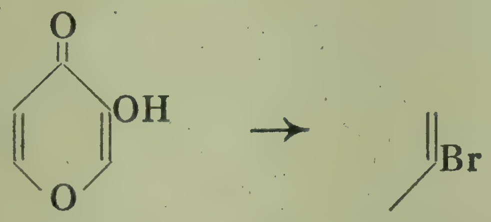


Br added with stirring to 100 gm. butyrolactone and red P, first at 20-30° with cooling, then at 70°, finally heated 3 hrs. at 80°, and excess Br blown off with air → 345 gm. α,γ-dibromobutyric acid bromide treated with water at 80° with vigorous stirring, and the acid so obtained heated 3 hrs. at 130-140° in vacuo until the gas evolution ceases → α-bromobutyrolactone (Y: 94%). H. Plieninger, B. *83*, 265 (1950).

Phosphoric acid/sodium acetate *H_3PO_4/CH_3COONa*

Bromination of acid-sensitive compounds

570.

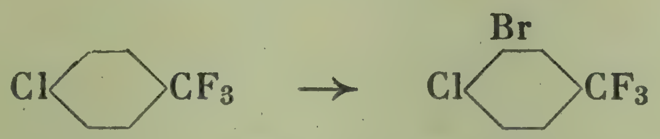


A soln. of pyromeconic acid in orthophosphoric acid treated at 0° with a soln. of Br_2 in saturated aq. Na-acetate → 2-bromopyromeconic acid. Y: up to 85%. High yields are obtained by using butter soln. to adjust the pH. E. L. Shimmin and F. Challenger, Soc. *1949*, 1185.

Antimony pentachloride *$SbCl_5$*

Bromination

571.



A soln. of Br_2 in 4-chloro(trifluoromethyl)benzene added slowly at 20° with cooling to $SbCl_5$, and Cl_2 introduced after the initial reaction has subsided → 3-bromo-4-chloro(trifluoromethyl)benzene. Y: 74.2%; conversion 31.1%.—Cl_2 reconverts Sb(III) salts into Sb(V)-chloride. Hydrolysis of the trifluoromethyl group to carboxyl occurs in the presence of Fe at 60°. F. e. s. E. T. McBee, R. A. Sanford, and P. J. Graham, Am. Soc. *72*, 1651 (1950).

Sulfuryl chloride *SO_2Cl_2*

Chlorination

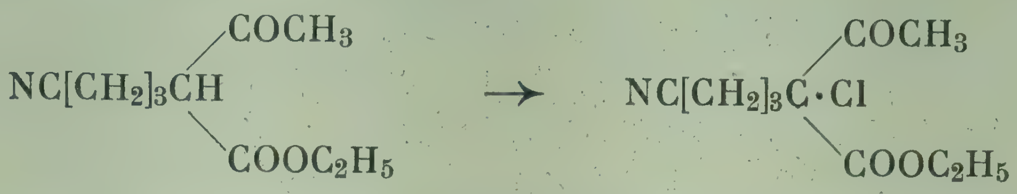
H → Cl

572. SO_2Cl_2 added in two portions to ethyl 4-hydroxybenzoate, and warmed on the steam bath for ca. 1.5 hrs. → ethyl 3,5-dichloro-4-hydroxybenzoate hydrate (startg. m. f. 136). Y: 83-88%. D. S. Tarbell, J. W. Wilson, and P. E. Fanta, Org. Synth. *29*, 35 (1949).

s. *1*, 417; s. a. D. F. Walker, J. Am. Pharm. Assoc. *39*, 396 (1950)

α-Chloro-*β*-ketocarboxylic acid esters from *β*-ketocarboxylic acid esters

573.



$$NC[CH_2]_3CH(COCH_3)(COOC_2H_5) \rightarrow NC[CH_2]_3C\cdot Cl(COCH_3)(COOC_2H_5)$$

SO_2Cl_2 added dropwise with stirring during 15 min. at 0-5° to ethyl 2-keto-6-cyanohexane-3-carboxylate in dry benzene, and after a further 15 min. refluxed 0.5 hr. → ethyl 3-chloro-2-keto-6-cyanohexane-3-carboxylate. Y: 87%. F. e. s. G. Swain, Soc. *1949*, 2898.

Sulfuric acid *H_2SO_4*

Iodination H → I

s. *4*, 492; s. a. D. Twiss and R. V. Heinzelmann, J. Org. Chem. *15*, 496 (1950)

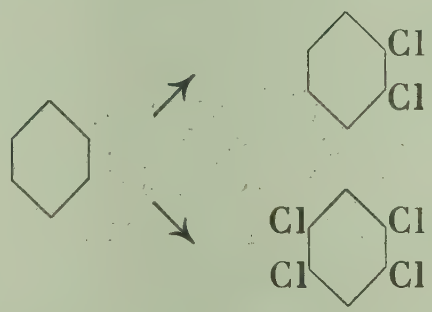
Iodine monochloride *ICl*

s. *1*, 419; 2, 493; *3*, 443; s. a. S. C. J. Olivier and W. P. Combé, R. *69*, 22 (1950)

Iodine trichloride *ICl_3*

Vicinal dichlorination CHCH → CClCCl

574.



Benzene and ICl_3 allowed to react in CCl_4 → o-dichlorobenzene (Y: 67%) and 1,2,4,5-tetrachlorobenzene (Y: 32%). F. e. s. E. Campaigne and W. Thompson, Am. Soc. *72*, 629 (1950).

Via intermediates *v.i.*

α-Bromoaldehydes from aldehydes H → Br
General method
Enol acetates from aldehydes
α-Bromoacetals from enol acetates
via α,β-bromoacetates
Cleavage of acetals

575. $RCH_2CHO \rightarrow RCH{=}CHOAc \rightarrow [RCHBrCHBrOAc] \rightarrow RCHBrCH(OCH_3)_2$
$\downarrow$
$R{=}CH_3[CH_2]_4\text{-}$ $RCHBrCHO$

A mixture of heptaldehyde, acetic anhydride, and powdered K-acetate heated 1 hr. at an oil-bath temp. of 155-160° → heptaldehyde enol acetate

(Y: 45-50%) dissolved in CCl_4, treated with shaking below 10° with a mixture of Br_2 and CCl_4 until the Br_2 is no longer decolorized, the brominated mixture added to anhydrous methanol, and allowed to stand for at least 48 hrs. → α-bromoheptaldehyde dimethyl acetal (Y: 80-85%) boiled gently with concd. HCl with distillation of the methanol liberated until the vapor temp. reaches 90°, the residue and distillate combined, and worked up → α-bromoheptaldehyde (Y: 90-95%). P. Z. Bedoukian, Org. Synth. *29*, 14 (1949).

Oxygen ↑ HalC ⇅ O

Without additional reagents *w.a.r.*

Chlorides from alcohols OH → Cl

s. *1*, 421; *4*, 497; s. a. E. Ziegler, M. *79*, 142 (1948)

Replacement of acoxy groups by bromine OAc → Br

s. *6*, 731

Lithium chloride *LiCl*

Chlorides from sulfonates OSO_2R → Cl

s. *5*, 402; s. a. M. F. Clarke and L. N. Owen, Soc. *1950*, 2108; G. Eglinton and M. C. Whiting, Soc. *1950*, 3650

Sodium iodide *NaI*

Iodides from sulfonates of carbohydrates OSO_2R → I

576. 6-Methanesulfonyl-1,2,3,4-diisopropylidene-D-galactose and NaI in acetone heated 40 hrs. at 130-135° → 1,2-3,4-diisopropylidene-6-iodo-6-desoxy-D-galactose. Y: 93%.—Other groups attached to the sugar molecule exercise a shielding effect on the tosyl and mesyl residues; this effect is greater for the latter smaller group. F. e. s. A. B. Foster et al., Soc. *1949*, 2542.

577. **of glycals.** The ethylene bond confers lability on a tosyloxy or mesyloxy group of the adjacent C-atom, so that a sec. tosyloxy group may be exchanged before a prim. one, which latter is usually more reactive. E. s. S. Laland, W. G. Overend, and M. Stacey, Soc. *1950*, 738.

Potassium iodide/phosphoric acid KI/H_3PO_4

s. Phosphoric acid/potassium iodide

Pyridine/phosphorus tribromide C_5H_5N/PBr_3

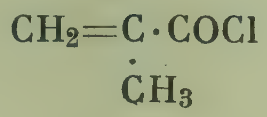
Bromides from alcohols OH → Br

s. *3*, 458; s. a. G. M. Badger et al., Soc. *1950*, 2326

Pyridine/benzenesulfonic acid chloride *$C_5H_5N/C_6H_5SO_2Cl$*

Carboxylic acid chlorides from carboxylic acids COOH → COCl

578.



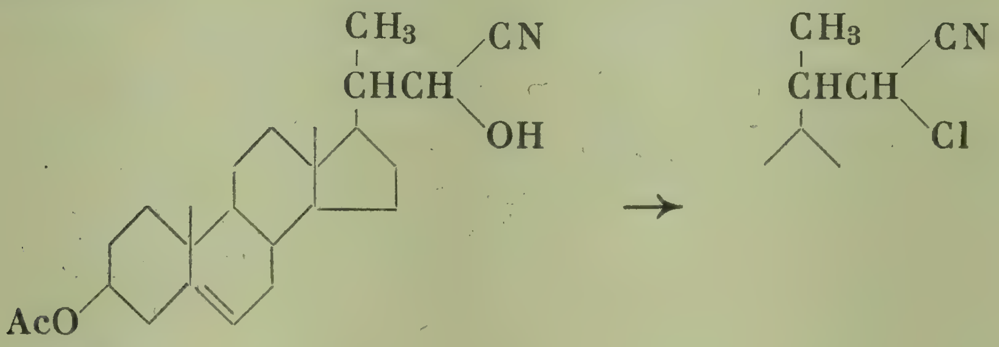
$CH_2=\underset{CH_3}{C}\cdot COCl$

A mixture of methacrylic acid and pyridine added with continuous shaking and cooling to benzenesulfonyl chloride, and distilled immediately → methacrylyl chloride (startg. m. f. NC ⇅ Hal. 6720). Y: 86%. J. Heyboer and A. J. Staverman, R. *69*, 787 (1950).

Lutidine/phosphorus oxychloride ←

α-Halogenonitriles from α-hydroxynitriles OH → Hal

579.

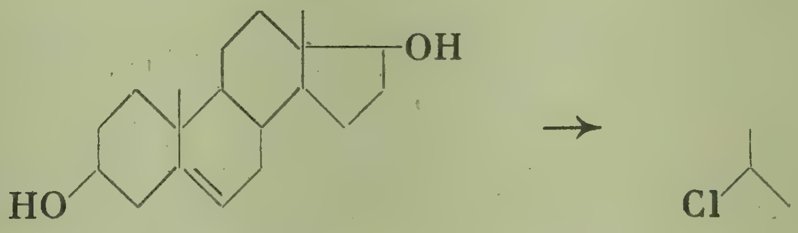


A mixture of 250 mg. 3β-acetoxybisnor-5-cholenaldehyde cyanohydrin and $POCl_3$ in lutidine gently refluxed for 10 min. → 250 mg. 22-cyano-22-chlorobisnor-5-cholen-3β-ol acetate. F. e. s. M. E. Herr and F. W. Heyl, Am. Soc. *72*, 1753 (1950).

Calcium carbonate/thionyl chloride *$CaCO_3/SOCl_2$*

Partial replacement of hydroxyl by chlorine OH → Cl

580.



500 mg. Δ^5-androstene-3β,17β-diol, dry $CaCO_3$, and a soln. of $SOCl_2$ in abs. benzene refluxed 1 hr. → 460 mg. Δ^5-3-chloroandrosten-17β-ol. C. A. Grob and W. A. Goldberg, Helv. *32*, 184 (1949).

Calcium chloride *$CaCl_2$*

Chlorides from alcohols

s. *6*, 812

Acetic acid *CH_3COOH*

Acylhalogenosugars OAc → Hal

s. *5*, 405; s. a. Am. Soc. *72*, 4173 (1950)

Benzoyl bromide *C_6H_5COBr*

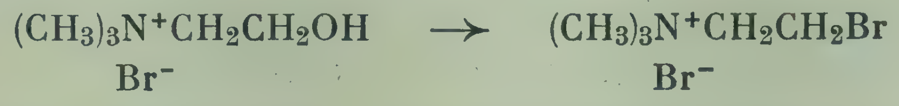
Carboxylic acid bromides COBr
C^{14}-Compounds

s. *5,* 566; s. a. C. Heidelberger and R. B. Hurlbert, Am. Soc. *72,* 4704 (1950)

α-Bromoisovaleryl bromide *$(CH_3)_2CHCHBrCOBr$*

Bromides from alcohols OH → Br

581.



$$\underset{Br^-}{(CH_3)_3N^+CH_2CH_2OH} \rightarrow \underset{Br^-}{(CH_3)_3N^+CH_2CH_2Br}$$

Choline bromide heated with α-bromoisovaleryl bromide to 110°, then the temp. raised to 140° during 2-3 hrs. → bromocholine bromide. Y: 75%. G. Kubiczek and L. Neugebauer, M. *80,* 395 (1949).

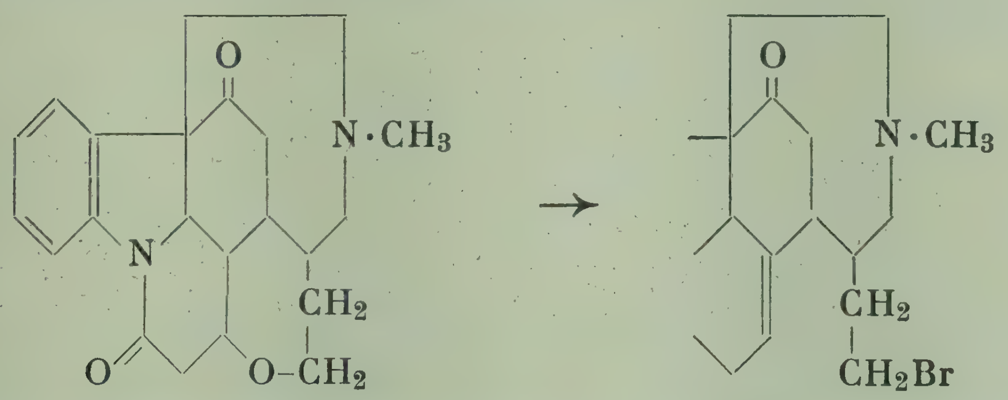
Phosphorus *P*

Acetobromosugars ←

582. Glucose added at 30-40° in the course of 0.5 hr. to acetic anhydride and a small amount of $HClO_4$, then amorphous P, and, gradually, below 20°, Br added, followed by 90% of the stoichiometric amount of water during 0.5 hr. with stirring, the flask closed, and left at room temp. for 1.5-2 hrs. → acetobromoglucose. Y: 85%. F. e. s. M. Bárczai-Martos and F. Körösy, Nature *165,* 369 (1950).

Ethylenebromides from O-heterocyclics C

583.

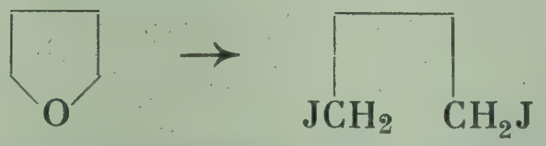


N-Methyldihydropseudostrychnine refluxed 5 hrs. at 130-140° with glacial acetic acid, red P, and fuming HBr → bromodesoxy-N-methyldihydroisopseudostrychnine hydrobromide (startg. m. f. 261). Y: ca. 100%. F. e. s. H.-G. Boit, B. *83,* 217 (1950); s. a. B. *84,* 16 (1951).

Phosphoric acid/potassium iodide *H_3PO_4/KI*

Iodides from ethers,
alcohols, and ethylene derivatives ←
Tetrahydrofuran ring opening

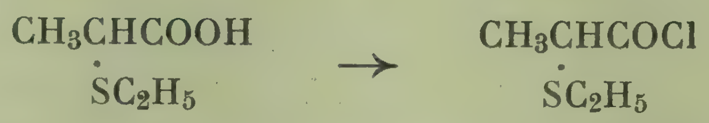
584.



Tetrahydrofuran and KI in 95%-H_3PO_4 refluxed 3 hrs. with stirring 1,4-diiodobutane. Y: 92-96%.—Similarly: Diisopropyl ether → isopropyl iodide. Y: 90%.—1,6-Hexanediol → 1,6-diiodohexane. Y: 83 to 85%.—2,3-Dimethyl-2-butene → 2,3-dimethyl-2-iodobutane. Y: 91.4%. —Excellent yields were obtained from various prim., sec., and tert. alcohols; phenols, however, were not converted into iodides. F. e. s. H. Stone and H. Shechter, Org. Synth. *30*, 33 (1950); *31*, 31, 66 (1951); J. Org. Chem. *15*, 491 (1950).

Phosphorus trichloride *PCl_3*

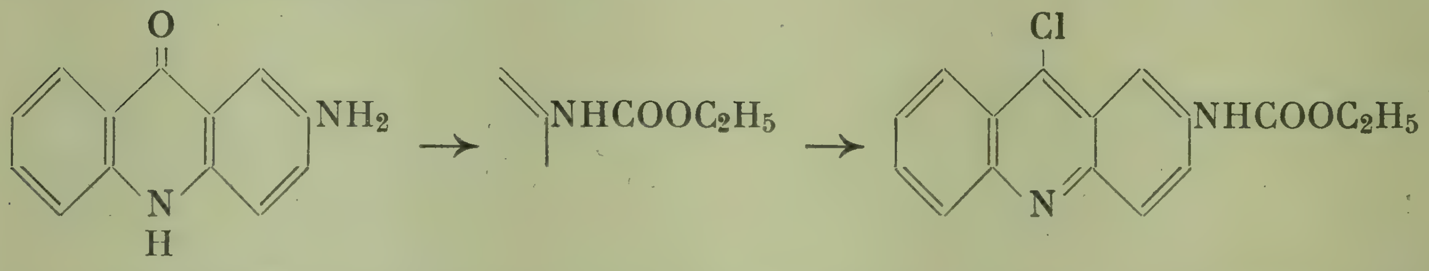
Carboxylic acid chlorides from carboxylic acids $COOH \rightarrow COCl$

585.

$$\underset{SC_2H_5}{CH_3\dot{C}HCOOH} \rightarrow \underset{SC_2H_5}{CH_3\dot{C}HCOCl}$$

A mixture of 2-ethylmercaptopropionic acid and PCl_3 allowed to stand overnight, then heated 1 hr. on a steam bath → 2-ethylmercaptopropionyl chloride. Y: 64%.—PCl_3 possesses the advantage that a colorless product is almost always obtained, and, in some instances, it gives a fair yield, when the use of $SOCl_2$ results in tar formation. From the viewpoint of yield, however, $SOCl_2$ is usually to be preferred. F. e. s. A. Mooradian et al., Am. Soc. *71*, 3372 (1949).

Phosphorus oxychloride *$POCl_3$*

9-Chloroacridines from acridones with protection of an amino group
Urethans from amines ←

586.


Freshly distilled ethyl chloroformate added to 2-aminoacridone and diethylaniline in boiling abs. alcohol, refluxed 30 min., concentrated to ⅓ of its volume, and poured into *N* HCl → 2-urethanoacridone (Y: 95%) refluxed with $POCl_3$ for 1 hr. → 9-chloro-2-urethanoacridine (Y: 87%). A. Albert and R. Royer, Soc. *1949*, 1148.

Phosphorus pentachloride *PCl_5*

Ethylene chlorides from ketones $COCH_2 \rightarrow CCl:CH$

s. *3*, 470; s. a. M. Mousseron and R. Jacquier, Bl. *1950*, 648; E. A. Braude and C. J. Timmons, Soc. *1950*, 2014

1,1-Dichlorides from ketones $CO \rightarrow CCl_2$

587. $C_6H_5COCF_3 \rightarrow C_6H_5CCl_2CF_3$

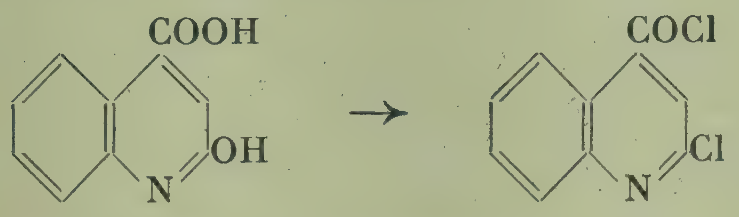
Trifluoroacetophenone and 50% excess PCl_5 refluxed 21 hrs. at an oil-bath temp. of 175°, acetone added to convert excess PCl_5 into $POCl_3$ for easier separation, and fractionated → α,α-dichloro-β,β,β-trifluoroethylbenzene. Y: 90%. F. e. s. S. G. Cohen, H. T. Wolosinski, and P. J. Scheuer, Am. Soc. *71*, 3439 (1949); *72*, 3952 (1950); s. a. L. J. Andrews and W. W. Kaeding, Am. Soc. *73*, 1007 (1951).

Carboxylic acid chlorides from carboxylic acids with simultaneous replacement of hydroxyl by chlorine

COOH → COCl

OH → Cl

588.



A mixture of 2-hydroxyquinoline-4-carboxylic acid (prepn. s. 723) and PCl_5 refluxed 1 hr. at 140-145° → 2-chloroquinoline-4-carboxylic acid chloride. Y: 98.5%. J. Büchi, H. Hurni, and R. Lieberherr, Helv. *32*, 1806 (1949); *33*, 858 (1950).

Iminochlorides from carboxylic acid amides

CONHR → C(:NR)Cl

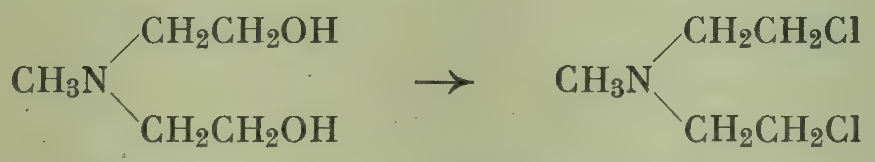
s. *6*, 441, 457

Thionyl chloride $SOCl_2$

Chloramines from aminoalcohols

OH → Cl

589.



$$CH_3N\begin{cases}CH_2CH_2OH\\CH_2CH_2OH\end{cases} \rightarrow CH_3N\begin{cases}CH_2CH_2Cl\\CH_2CH_2Cl\end{cases}$$

A soln. of pure N-methyldiethanolamine in trichloroethylene added with stirring during 1 hr. to a mixture of $SOCl_2$ and trichloroethylene at 50°, and refluxed for 2 hrs. → N-methyl-2,2′-dichlorodiethylamine. Y: 95%, purity 96%. Variation of reaction conditions and solvents s. J. T. Abrams et al., J. Soc. Chem. Ind. *68*, 280 (1949); s. a. J. H. Burckhalter, V. C. Stephens, and L. A. R. Hall, J. Am. Pharm. Assoc. *39*, 271 (1950).

Carboxylic acid chlorides from carboxylic acids

COOH → COIC

s. *6*, 585; s. a. O. T. Schmidt and A. Schach, A. *571*, 29 (1951)

Sulfuric acid H_2SO_4

Replacement of hydroxyl by bromine

OH → Br

s. *1*, 437; s. a. S. Bezzi and P. Lanza, G. *80*, 180 (1950)

Fluorosulfonic acid *FSO_3H*

Sulfonic acid fluorides SO_2F

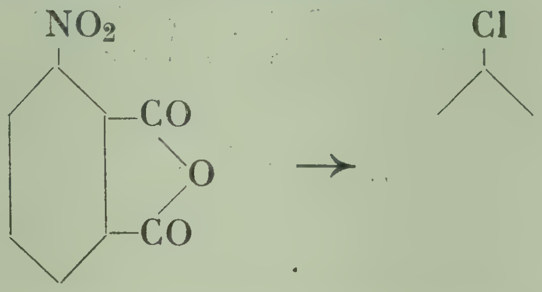
590. A mixture of dry crude Na-p-chlorobenzenesulfonate, fluorosulfonic acid, and CCl_4 stirred and heated at 70-75° for 24 hrs. → p-chlorobenzenesulfonyl fluoride. Y: 85%. F. e. s. M. Kulka, Am. Soc. *72,* 1215 (1950).

Nitrogen ↑ HalC ⇅ N

Without additional reagents *w.a.r.*

Replacement of nitro groups by chlorine $NO_2 \rightarrow Cl$

591.

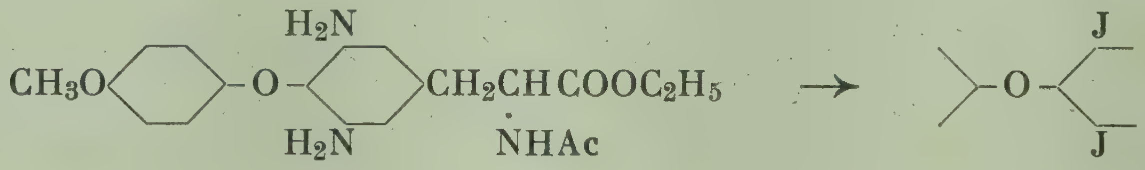


22 gm. 3-nitrophthalic anhydride treated with Cl_2 at 230-250° for 6-7 hrs. → 15-15.5 gm. 3-chlorophthalic anhydride. F. e. s. A. A. Ponomarenko, Ж. *20,* 469 (1950); C. A. *44,* 7810b.

Sodium nitrite *$NaNO_2$*

Iodides from amines $NH_2 \rightarrow I$

592.



A soln. of 3,5-diamino-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester in acetic acid-H_2SO_4 added dropwise during ca. 2 hrs. with stirring and cooling to a soln. of $NaNO_2$ in glacial acetic acid-H_2SO_4, stirring continued for 1 hr. at 0°, added fairly rapidly without cooling to a well stirred soln. of NaI, iodine, and urea in water over a layer of chloroform, and stirring continued for 1 hr. → 3,5-diiodo-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester (startg. m. f. 26). Y: 82%.—The chloroform, which extracts the reaction product, avoids the formation of solid or semi-solid matter during the reaction. J. R. Chalmers et al., Soc. *1949,* 3424.

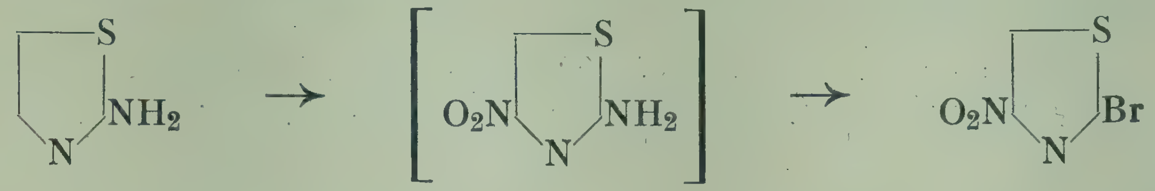
Potassium iodide *KI*

s. *1,* 438; *2,* 522; s. a. S. C. J. Olivier and W. P. Combé, R. *69,* 22 (1950)

Copper *Cu*

Nitration with subsequent replacement of amino groups by halogen ←

593.



HNO_3 (d.1.51) added dropwise with stirring to a soln. of 30 gm. 2-aminothiazole in concd. H_2SO_4, after 12 hrs. the mixture and Gattermann-Cu added simultaneously at 15° to aq. NaBr, then diazotized with aq. $NaNO_2$ at 10-15° over a period of 20 min. with stirring — 33 gm. 2-bromo-5-nitrothiazole. H. v. Babo and P. Prijs, Helv. *33*, 306 (1950).

Fluoboric acid *HBF_4*

Fluorides from amines
Schiemann reaction $NH_2 \rightarrow F$

s. *3*, 478; *4*, 509; s. a. G. C. Finger, Am. Soc. *73*, 149 (1951) and other papers of this series

Halogen ↑ HalC ⇅ Hal

Without additional reagents *w.a.r.*

Chlorides from bromides Br → Cl

s. *5*, 413; s. a. G. Fawaz and L. F. Fieser, Am. Soc. *72*, 996 (1950); H. J. den Hertog and J. de Bruyn, R. *70*, 182 (1951); F. Arndt et al., B. *84*, 319 (1951)

Sodium iodide *NaI*

Iodides from other halides
Finkelstein reaction Hal → I

s. *1*, 450; *4*, 512; in ethyl methyl ketone s. *6*, 906; E. Klingsberg, Am. Soc. *72*, 1031 (1950)

Antimony pentachloride *$SbCl_5$*

Fluorides from chlorides Cl → F

s. *4*, 514; s. a. E. T. McBee and R. A. Sanford, Am. Soc. *72*, 5574 (1950)

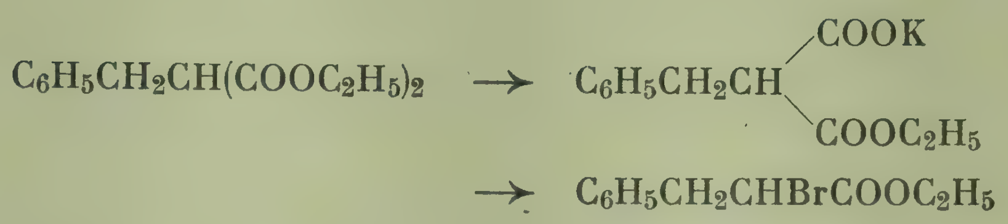
Carbon ↑

HalC ⇅ C

Potassium salt *K+*

α-Bromocarboxylic acid esters from malonic esters ←

594.



$$C_6H_5CH_2CH(COOC_2H_5)_2 \rightarrow C_6H_5CH_2CH\begin{matrix}\diagup COOK\\ \diagdown COOC_2H_5\end{matrix} \rightarrow C_6H_5CH_2CHBrCOOC_2H_5$$

A soln. of KOH in abs. alcohol added with stirring to a soln. of diethyl benzylmalonate, allowed to stand several hrs. at room temp., filtered, the alcohol distilled off, the remaining K ethyl benzylmalonate dried, finely pulverized, mixed with CCl_4, and the stirred ice-cold mixture treated with a soln. of Br_2 in CCl_4 during 2-4 hrs. → ethyl α-bromo-β-phenylpropionate. Y: 80%. F. e. with lower yields s. J. R. Dice and J. N. Bowden, Am. Soc. *71*, 3107 (1949).

Silver salt *Ag+*

Halides from carboxylic acids Degradation with loss of 1 C-atom COOH → Hal

s. *1*, 453/4; *3*, 489; *4*, 517; s. a. A. L. Henne and W. G. Finnegan, Am. Soc. *72*, 3806 (1950); A. C. Cope and M. E. Synerholm, Am. Soc. *72*, 5228 (1950); M. Heintzeler, A. *569*, 102 (1950); R. N. Haszeldine, Soc. *1951*, 584; pure sec. bromides s. J. Cason and R. H. Mills, Am. Soc. *73*, 1354 (1951); in trichloroethylene s. M. Stoll and A. Rouvé, Helv. *34*, 98 (1951)

595. **Effect of nitro groups.** Competing reactions, i.e. nuclear and side chain bromination, can be minimized by introduction of nitro groups into the nucleus. E. s. R. A. Barnes and R. J. Prochaska, Am. Soc. *72*, 3188 (1950); W. G. Dauben and H. Tilles, Am. Soc. *72*, 3185 (1950).

Sodium hypobromite *NaOBr*

Halides from α-ketocarboxylic acid esters COCOOR → Hal

596. $C_6H_5CH(CN)COCOOC_2H_5 \rightarrow C_6H_5CH(CN)Br$

An ice-cold mixture of Br_2, NaOH, and water added at 0° to a soln. of ethyl phenylcyanopyruvate in aq. NaOH → phenylbromoacetonitrile. Y: 82%. F. e. s. S. Wideqvist, Am. Soc. *71*, 4152 (1949).

Formation of S—S Bond

Exchange

Hydrogen ↑ SS ⇅ H

Potassium ferricyanide *$K_3[Fe(CN)_6]$*

Sym. disulfides from mercaptans 2 RSH → RS·SR

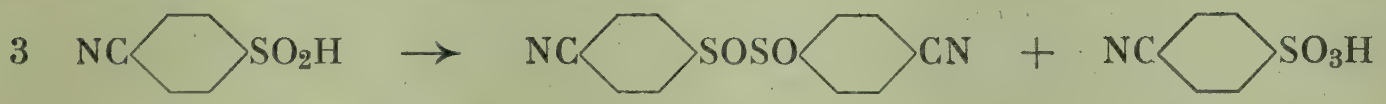
597. $2\ C_6H_5SH \rightarrow C_6H_5S\cdot SC_6H_5$

A soln. of thiophenol in aq. NaOH oxidized with K-ferricyanide → diphenyl disulfide. Y: almost 100%. V. O. Lukashevich and M. M. Sergeeva, Ж. *19,* 1493 (1949); C. A. *44,* 3451i.

Oxygen ↑ SS ⇅ O

Hydrochloric acid *HCl*

Sym. disulfoxides from sulfinic acids $2\ RSO_2H \rightarrow RSO\cdot SOR$

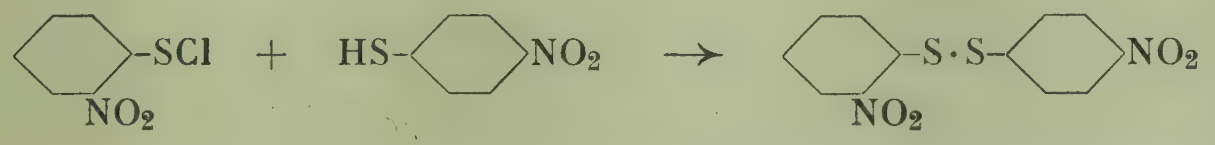
598. 

An aq. soln. of Na-p-cyanobenzenesulfinate cooled to 0°, acidified strongly with concd. HCl, and kept 2 days at 0° → di-p-cyanophenyl disulfoxide. Y: 70%. L. Bauer and J. Cymerman, Soc. *1950,* 109.

Halogen ↑ SS ⇅ Hal

Without additional reagents *w.a.r.*

Disulfides from sulfenylchlorides ←

599. 

o-Nitrophenyl sulfenylchloride mixed with p-nitrophenylmercaptan in ether, and worked up on the next day → 2,4′-dinitrophenyl disulfide. Y: 88%. F. e. s. V. O. Lukashevich and M. M. Sergeeva, Ж. *19,* 1493 (1949); C. A. *44,* 3451i. In the presence of NaOH s. F. D. Stuart and R. A. Mathes, J. Org. Chem. *14,* 1111 (1949).

Lithium aluminum hydride *$LiAlH_4$*

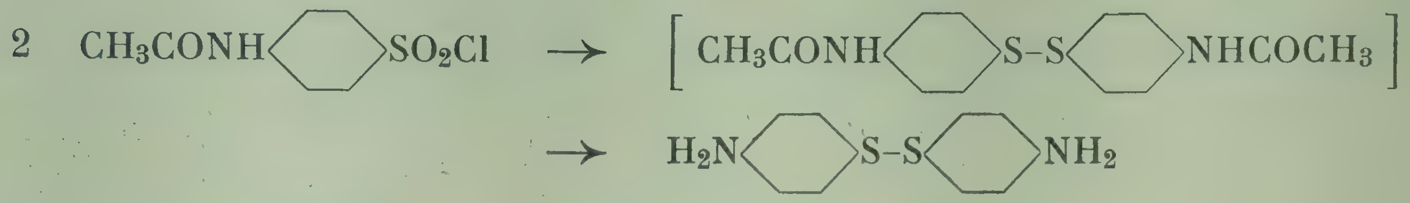
Sym. disulfides from sulfenylchlorides 2 RSCl → RS·SR

s. *6,* 47

Hydriodic acid *HI*

Sym. disulfides from sulfonic acid chlorides $2\ RSO_2Cl \rightarrow RS{\cdot}SR$

600.



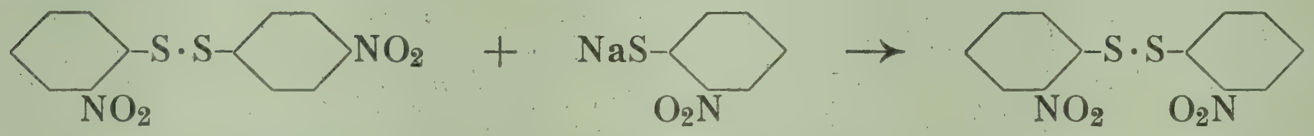
p-Acetamidobenzenesulfonyl chloride and HI (d. 1.72) in glacial acetic acid allowed to stand at room temp. for 22 hrs., diluted with Na-thiosulfate soln., and worked up, whereby the amino group is deacylated by refluxing 1.5 hrs. with concd. HCl-alcohol → di-p-aminophenyl disulfide. Y: 77.5%. F. e. s. L. Bauer and J. Cymerman, Soc. *1949*, 3434.

Sulfur ↑ SS ⇅ S

Sodium salt *Na^+*

Reactions with di- and tri-sulfides ←

601.



A suspension of 2,4′-dinitrodiphenyl disulfide in methanol treated with a soln. of Na-2-nitrophenylmercaptide in methanol, and shaken 1 hr. at room temp. → 2,2′-dinitrodiphenyl disulfide. Y: 82.3%. F. e. s. V. O. Lukashevich and M. M. Sergeeva, Ж. *19*, 1493 (1949); C. A. *44*, 3451i.

Formation of S—Rem Bond

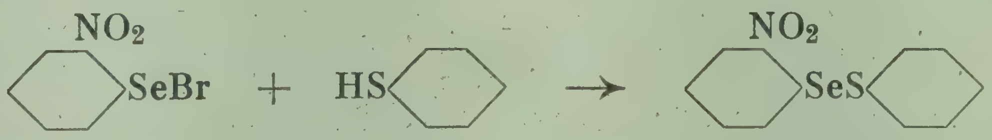
Exchange

Halogen ↑ SRem ⇅ Hal

Without additional reagents *w.a.r.*

Selenylsulfides from selenylhalides ←

602.

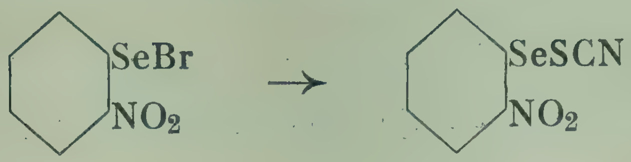


o-Nitrophenyl selenylbromide triturated with thiophenol, then allowed to stand 24 hrs. at room temp. → o-nitrophenylselenyl phenyl sulfide (startg. m. f. 159, 666). Y: 97.4%. F. methods and e. s. H. Rheinboldt and E. Giesbrecht, A. *568*, 198 (1950).

Potassium salt *K+*

Selenylthiocyanates from selenylhalides SeHal → SeSCN

603.



A soln. of o-nitrophenylselenyl bromide in dry benzene agitated 3 hrs. at room temp. with K-thiocyanate and some glass beads → o-nitrophenylselenyl thiocyanate. Y: ca. 100%. F. e. and reactions s. H. Reinboldt and M. Perrier, Bl. *1950*, 245.

Formation of S—C Bond

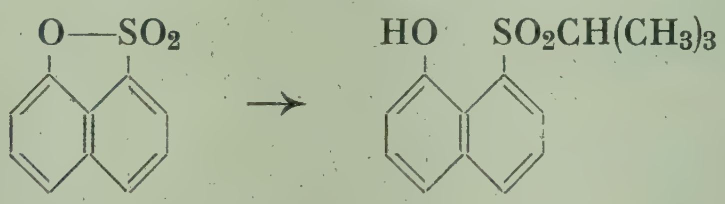
Uptake

Addition to Oxygen and Sulfur SC⇓OS

Magnesium *Mg*

Hydroxysulfones from sultones ⊂

604.



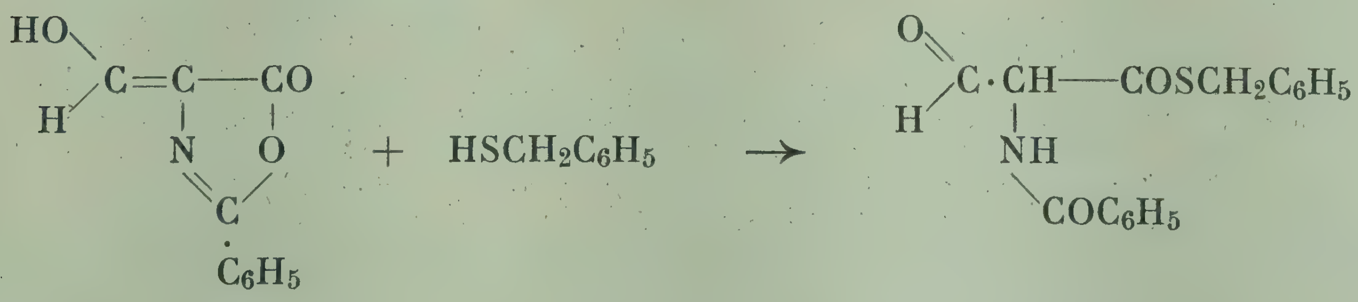
Naphthosultone in dry benzene added to an ethereal soln. of *tert*-butyl-MgBr, refluxed for 4 hrs., then set aside overnight → 8-*tert*-butylsulfonyl-1-naphthol. Y: ca. 75%. F. e. s. A. Mustafa, Soc. *1949*, 2151.

Addition to Oxygen and Carbon SC⇓OC

Sodium *Na*

Oxazolone ring opening ⊂

605



2-Phenyl-4-hydroxymethylene-5-oxazolone heated at 100° with benzyl mercaptan and a small piece of Na for 0.5 hr. → benzyl phenylthiopenaldate. Y: ca. 100%. E. V. Brown, Chemistry of Penicillin *1949*, 516.

Sodium salt Na^+

Hydroxythioethers from oxido compounds
Carbohydrates

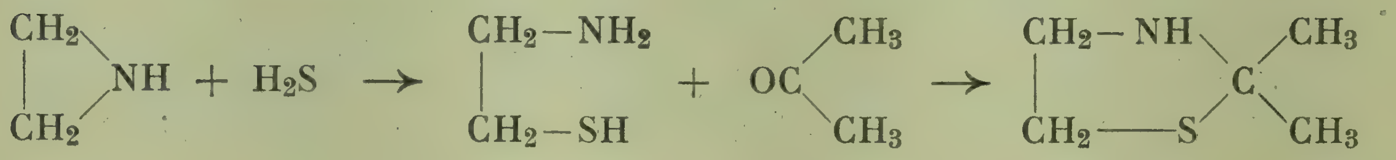
s. *2*, 532; s. a. F. H. Newth, G. N. Richards, and L. F. Wiggins, Soc. *1950*, 2356

Addition to Nitrogen and Carbon SC ⇓ NC

Without additional reagents *w.a.r.*

Aminomercaptans and thiazolidines from cyclic imines ←

606.



Ethyleneimine added at –70 to –60° to a soln. of H_2S in methanol, and allowed to warm gradually to room temp. → β-mercaptoethylamine. Y: 70–80%.

H_2S introduced at 10–20° with stirring into a soln. of ethyleneimine in acetone over a period of 3 hrs., and stirring continued at room temp. for several hrs. → 2,2-dimethylthiazolidine. Y: 90%.

F. e. and reactions with ethyleneimine s. H. Bestian, A. *566*, 210 (1950); aminomercaptans s. a. G. J. Braz, Ж. *21*, 688 (1951); C. A. *45*, 9473e.

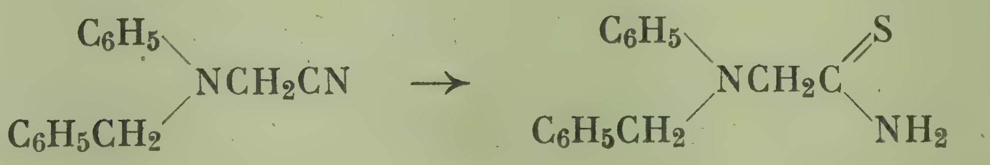
Sodium/alcohol *NaOR*

Carboxylic acid thioamides from nitriles CN → $CSNH_2$

s. *6*, 608

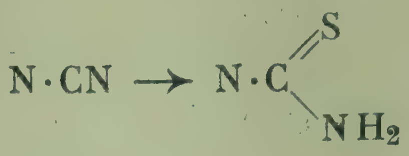
Ammonia NH_3

607.



N-Benzyl-N-phenylglycinonitrile, NH_3, and H_2S in methanol heated 1 hr. at 70° in a pressure bottle → N-benzyl-N-phenylaminoacetothioamide. Y: 97%. F. e. s. R. A. Turner and C. Djerassi, Am. Soc. *72*, 3081 (1950).

Thioureas from cyanamides

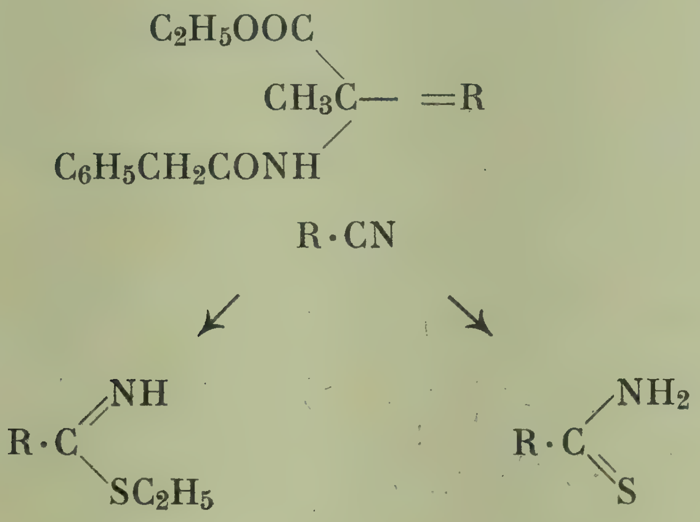


s. *4*, 532; s. a. F. Kurzer, Soc. *1950*, 3269

Hydrochloric acid *HCl*

Iminothiolic esters and carboxylic acid thioamides from nitriles ←

608.



α-Phenylacetamido-α-carbethoxypropionitrile

(4.6 g.) in dry ether and ethylmercaptan saturated at 0^0 with dry HCl, kept 24 hrs. at the same temp., evaporated, redissolved in chloroform, and shaken with aq $NaHCO_3$ → 3 g. → α-phenylacetamido-α-carbethoxypropionimino ethyl thioether.

(1 g.) added to a soln. of Na in ethanol, which has been saturated at -10^0 with H_2S, and heated 6 hrs. at 50–60^0 in a closed vessel → 0.85 g. α-phenylacetamido-α-carbethoxypropionothioamide.

A. H. Cook et al., Soc. *1949*, 3220; thioamides s. a. R. Dahlbom, Acta Chem. Scand. *4*, 744 (1950).

Addition to Halogen and Sulfur SC ⇓ HalS

Without additional reagents *w.a.r.*

Chlorothioethers from sulfenylchlorides ←

609. $ClCH_2SCl + CH_2{=}CH_2 \rightarrow ClCH_2SCH_2CH_2Cl$

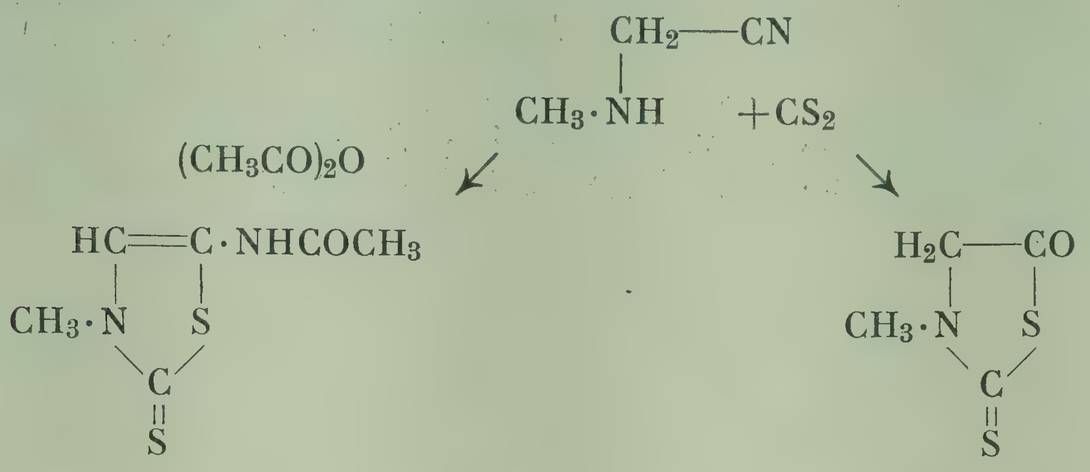
A slow stream of ethylene introduced into chloromethyl sulfenylchloride below 50^0 until the soln. is colorless → chloromethyl β-chloroethyl sulfide. Y: ca. 100%. H. Brintzinger et al., Chem. B. *83*, 87 (1950).

Addition to Sulfur and Carbon SC ⇓ SC

Without additional reagents *w.a.r.*

Thiazole ring from α-aminonitriles ○

610.



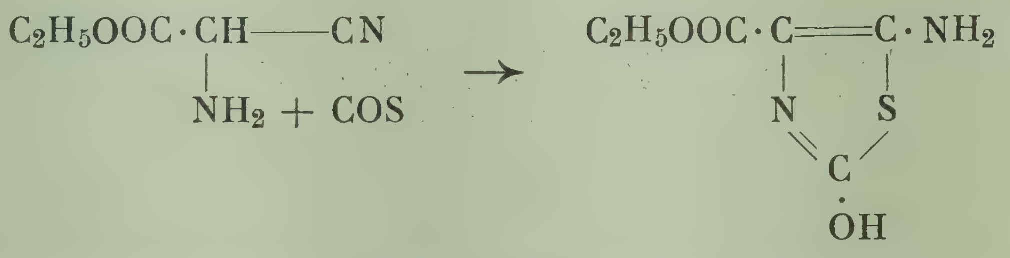
Methylaminoacetonitrile

in ethyl acetate added under N_2 with cooling and stirring to CS_2, then treated with acetic anhydride → 5-acetamido-2-thio-3-methylthiazoline (startg. m. f. 378). Y: 74%.

in methanol added under N_2 with cooling and stirring to CS_2 in methanol, after 30 min. treated with KOH in methanol, kept at 0^0 for *24* hrs., evaporated in vacuo, dissolved in water, and treated with concd. HCl → 2-thio-3-methylthiazolid-5-one (startg. m.f. 362). Y: 78%.

A. H. Cook and S. F. Cox, Soc. *1949*, 2337.

611.



5-Amino-2-hydroxythiazoles. Ethyl aminocyanoacetate in ether treated with excess carbon oxysulfide, which is bubbled into the soln. during 6 hrs. → 5-amino-2-hydroxy-4-carbethoxythiazole. Y: 96%. F. e. s. A. H. Cook, I. Heilbron, and G. D. Hunter, Soc. *1949*, 1443.

Potassium hydroxide/alcohol *KOH*

s. *6*, 610

Addition to Carbon SC ⇓ CC

Without additional reagents *w.a.r.*

Thioethers from ethylene derivatives C:C → CHCSR

612. The highest rate of addition of ethyl mercaptan to 1-hexadecene is obtained by using ultraviolet light of the proper wave length. Catalysts and inhibitors, s. J. T. Hackmann and R. Berkenbosch, R. *68*, 745 (1949).

Cyanoethyl hydroxyalkyl thioethers from vinyl cyanides

613. $HOCH_2CH_2SH + CH_2{=}CHCN \rightarrow HOCH_2CH_2SCH_2CH_2CN$

Acrylonitrile added with stirring to 2-mercaptoethanol, a small portion added at first, then warmed at 35-40° for 5 min., a second portion added dropwise during 10 min. at 55-60°, and a final portion added all at once, then stirred 16 hrs. at room temp. → β-(2-hydroxyethylmercapto)propionitrile. Y: 92-94%. L. L. Gershbein and C. D. Hurd, Org. Synth. *29*, 52 (1949).

β-Ketosulfones from α,β-ethyleneketones $C{:}C \rightarrow CHCSO_2R$

s. *4*, 535; cf. H. Gilman and L. F. Cason, Am. Soc. *72*, 3469 (1950)

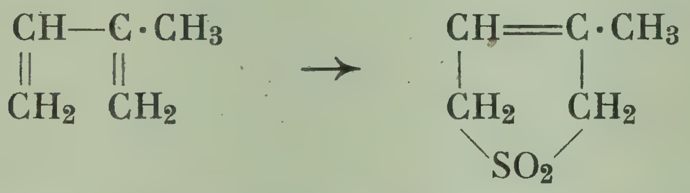
Addition of thiolic acids to carbon double and triple bonds ←

614. $C_6H_{11}C{\equiv}CH \rightarrow C_6H_{11}CH{\equiv}CHSCOCH_3$

Thioacetic acid added dropwise to cyclohexylacetylene on a water bath, then heated 2 hrs. more → 2-cyclohexylvinyl thiolacetate. Y: 96%. F. e., also addition of 2 mole thiolic acid, s. H. Behringer, A. *564*, 219 (1949).

Sulfones from dienes ○

615.

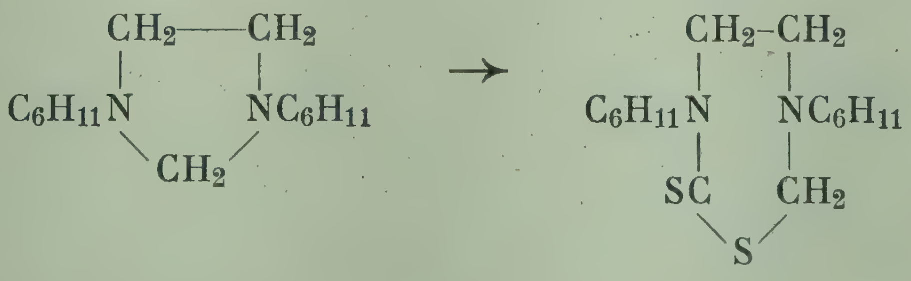


A precooled autoclave charged with isoprene, liq. SO_2, methanol, and some hydroquinone, sealed, heated slowly to 85°, and maintained at that temp. for 4 hrs. → 3-methyl-2,5-dihydrothiophene-1,1-dioxide. Y: 77-87% depending on the purity of isoprene. F. e. s. R. L. Frank and R. P. Seven, Org. Synth. *29*, 59 (1949).

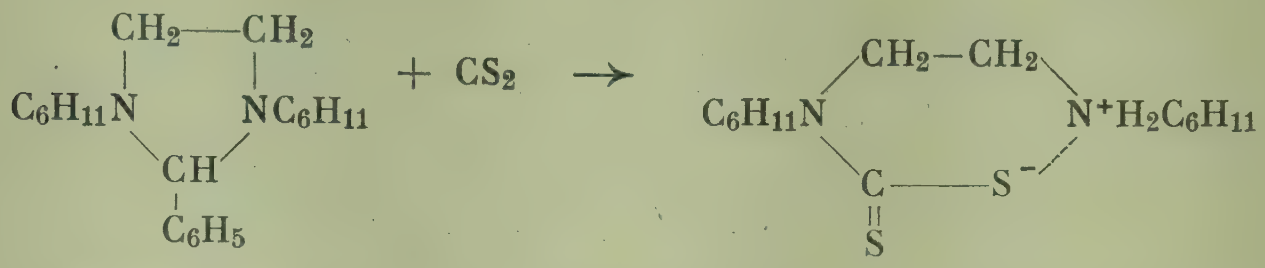
s. a. *1*, 459, 713; O. Grummitt, A. E. Ardis, and J. Fick, Am. Soc. *72*, 5167 (1950)

Hexahydro-1,3,6-thiadiazepine-2-thiones and amino-dithiocarbamic acids from imidazolines ←
Ring enlargement

616.



CS_2 added to a soln. of 1,3-dicyclohexylimidazolidine (prepn. s. 404) in alcohol, and allowed to stand at room temp. for 2 hrs. → 3,6-dicyclohexyl-hexahydro-1,3,6-thiadiazepine-2-thione. Y: 97%.

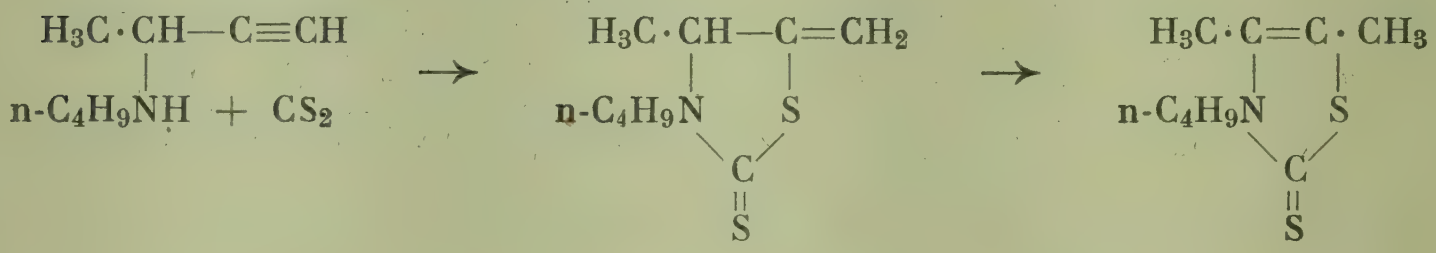


2.5 gm. CS_2 added slowly to an agitated soln. of 9.8 gm. 1,3-dicyclohexyl-2-phenylimidazolidine in alcohol, and worked up after 2 hrs. → 8.9 gm. N-cyclohexyl-N-(β-cyclohexylaminoethyl)dithiocarbamic acid inner salt.—The different course of the reaction is caused by substitution in position 2. F. e. s. R. A. Donia et al., J. Org. Chem. *14*, 952 (1949).

Sodium hydroxide *NaOH*

5-Methyl-2(3H)-thiazolethiones from acetyleneamines via 5-methylene-2-thiazolidinethiones ←

617.



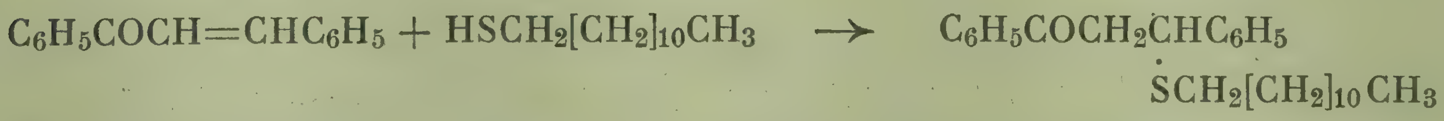
CS_2 added dropwise during 1 hr. to a well-stirred mixture of NaOH, water, and 2-n-butylamino-3-butyne at 50°, and stirring continued for a further 2 hrs. → 4-methyl-3-n-butyl-5-methylene-2-thiazolidinethione (Y: 87%) dissolved in concd. H_2SO_4, and poured on crushed ice → 4,5-dimethyl-3-n-butyl-2(3H)-thiazolethione (Y: 86%). F. e. s. J. W. Batty and B. C. L. Weedon, Soc. *1949*, 786.

Sodium/alcohol *NaOR*

β-Ketothioethers from α,β-ethyleneketones

C:C → CHCSR

618.



$$C_6H_5COCH{=}CHC_6H_5 + HSCH_2[CH_2]_{10}CH_3 \longrightarrow C_6H_5COCH_2\underset{SCH_2[CH_2]_{10}CH_3}{C}HC_6H_5$$

A little 2 *N* Na-ethoxide added to a mixture of benzylideneacetophenone, n-dodecyl mercaptan, and benzene, vigorously shaken, and allowed to stand for 12 hrs. → benzylacetophenone β-n-dodecyl sulfide. Y: 95%. F. e. s. F. Kipnis and J. Ornfelt, Am. Soc. *71*, 3554 (1949).

Sodium acetate *CH_3COONa*

Sym. thioethers from ethylene derivatives ←

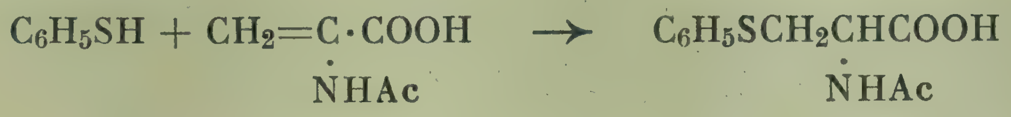
619. $2\ CH_2{=}CHCOOC_2H_5 + H_2S \longrightarrow S(CH_2CH_2COOC_2C_5)_2$

H_2S introduced over a period of 25 hrs. into a boiling soln. of methyl acrylate, Na-acetate trihydrate, and 95%-ethanol → methyl β-thiodipropionate. Y: 71-81%. E. A. Fehnel and M. Carmack, Org. Synth. *30*, 65 (1950).

Piperidine *$C_5H_{11}N$*

Thioethers from ethylene derivatives C:C → CHCSR
Mercapturic acids

620.

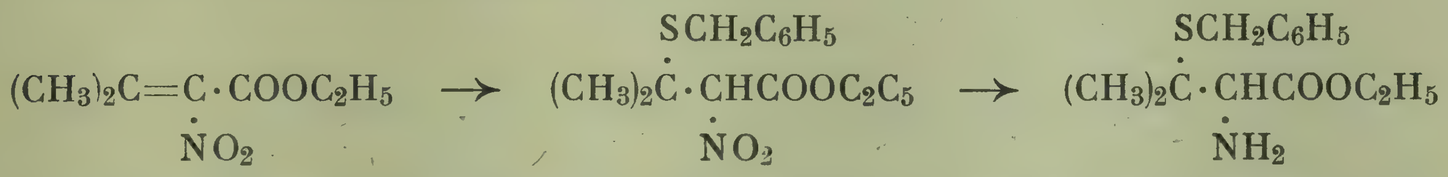


$$C_6H_5SH + CH_2{=}\underset{NHAc}{C}\cdot COOH \longrightarrow C_6H_5SCH_2\underset{NHAc}{C}HCOOH$$

Acetaminoacrylic acid, thiophenol, and piperidine in dioxane refluxed 1 hr. → rac. phenylmercapturic acid. Y: 86%. F. e. s. H. Behringer and E. Fackler, A. *564*, 73 (1949); cyanosulfides s. R. M. Ross, H. L. Bushey, and R. J. Rolih, Am. Soc. *73*, 540 (1951).

β-Alkylthio-α-aminocarboxylic acid esters from α-nitro-α,β-ethylenecarboxylic acid esters via β-alkylthio-α-nitrocarboxylic acid esters

621.



$$(CH_3)_2C{=}\underset{NO_2}{C}\cdot COOC_2H_5 \longrightarrow (CH_3)_2\overset{SCH_2C_6H_5}{C}\cdot\underset{NO_2}{C}HCOOC_2C_5 \longrightarrow (CH_3)_2\overset{SCH_2C_6H_5}{C}\cdot\underset{NH_2}{C}HCOOC_2H_5$$

A soln. of benzylmercaptan in abs. methanol treated with piperidine, cooled to 0°, ethyl α-nitrodimethylacrylate (prepn. s. 382) added during 1 hr., allowed to stand 6 hrs. at 0°, then 48 hrs. at 20°, then 48 hrs. at 20°, neutralized with acetic acid, methanol distilled off in vacuo, the residue, containing ethyl α-nitro-β-(benzylmercapto)isovalerate, dissolved in ethanol, powdered Sn addded, then treated slowly with 37%-HCl at 20-25° with vigorous stirring during 4-6 hrs., stirring continued until the Sn has disappeared, and worked up via the chlorostannate → ethyl α-amino-β-(benzylmercapto)isovalerate. Y: ca. 70%. R. Trave, G. *79*, 233 (1949).

Hydroquinone ←

Sulfones from dienes ○
s. *6*, 615

Hydrochloric acid *HCl*

1,6-Addition ←
s. *6*, 655

Exchange

Hydrogen ↑ SC ⇅ H

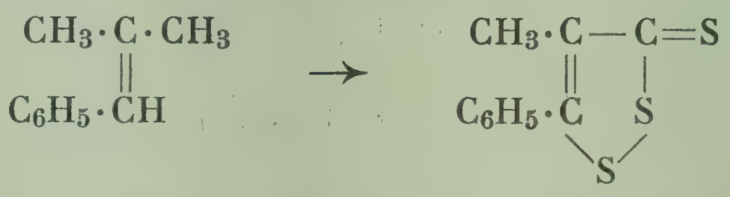
Without additional reagents *w.a.r.*

Sulfochlorination H → SO_2Cl

s. *2*, 538; *3*, 511; s. a. H. Y. Lew and C. R. Noller, Am. Soc. *72*, 5715 (1950); J. A. Solov'eva and G. J. Arbuzov, Ж. *21*, 765 (1951); C. A. 45, 9524i

1,2-Dithioles from ethylene derivatives ○

622.

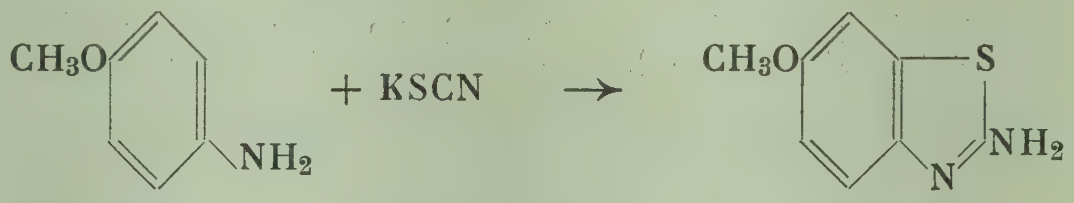


2-Methyl-1-phenylpropene heated with S to 190°, and kept 10 hrs. at 190-210° → 4-methyl-5-phenyl-1,2-dithiole-3-thione. Y: 80%. F. e. s. M. G. Voronkov, A. S. Broun, and G. B. Karpenko, Ж. *19*, 1927 (1949); C. A. *44*, 1955g.

Potassium thiocyanate *KSCN*

2-Aminobenzothiazoles

623.



A soln. of Br_2 in glacial acetic acid added dropwise with stirring below 35° to a soln. of p-anisidine and K-thiocyanate in 96% acetic acid, then stirred for 10 hrs. → 2-amino-6-methoxybenzothiazole. Y: 87%. C. G. Stuckwisch, Am. Soc. *71*, 3417 (1949).

Pyridine-sulfur trioxide *$C_5H_5N{\cdot}SO_3$*

Sulfonation H → SO_3H

of heterocyclics s. *3*, 508; of dienes s. Ж. *21*, 704; C. A. *45*, 8969f

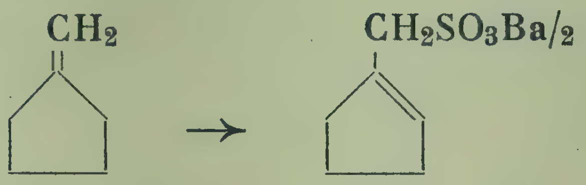
Mercuric sulfate *$HgSO_4$*

s. *2*, 540; s. a. S. Maffei, G. *80*, 651 (1950)

Dioxane/sulfur trioxide ←

Replacement of hydrogen by sulfonic acid groups with rearrangement ←

624.

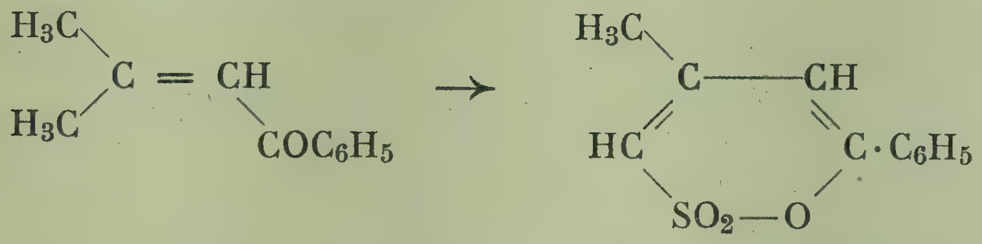


A soln. of methylenecyclopentane in ethylene chloride added with vigorous stirring at —5 to 0° over a period of 40 min. to a suspension of dioxane-SO_3 complex in ethylene chloride, the following day decomposed with ice-water, and the aq. phase neutralized by careful addition of Ba-carbonate → Ba-1-cyclopentenylmethanesulfonate. Y: 97%. F. reactions with migration of the double bond into the ring s. R. T. Arnold, R. W. Amidon, and R. M. Dodson, Am. Soc. *72*, 2871 (1950); without rearrangement s. R. Sperling, Soc. *1949*, 1925; oxo compounds s. W. E. Truce and C. C. Alfieri, Am. Soc. *72*, 2740 (1950).

Acetic anhydride $(CH_3CO)_2O$

Sultones from ethylene ketones ○

625.



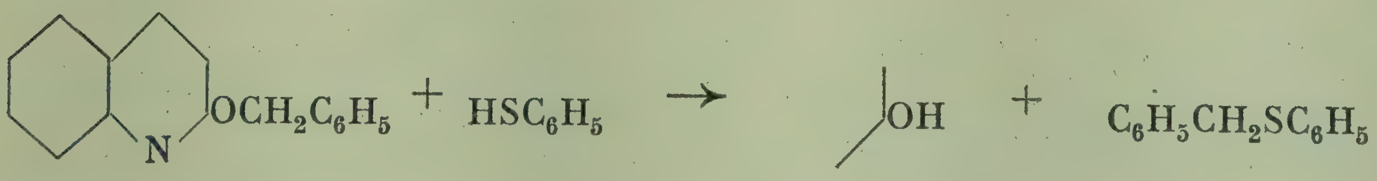
H_2SO_4 (d. 1.84) followed by isopropylideneacetophenone added dropwise with ice-salt cooling and vigorous stirring below 0° to acetic anhydride, then kept at —5° for 24 hrs. and at room temp. for another 24 hrs. → 2-methyl-4-phenyl-4-buta-1,3-dien-4-ol-1-sulfonic acid sultone. Crude: Y: 84%. F. e. s. T. Morel and P. E. Verkade, R. *68*, 619 (1949).

Oxygen ↑ SC ⇵ O

Without additional reagents *w.a.r.*

Cleavage of ethers by mercaptans ←

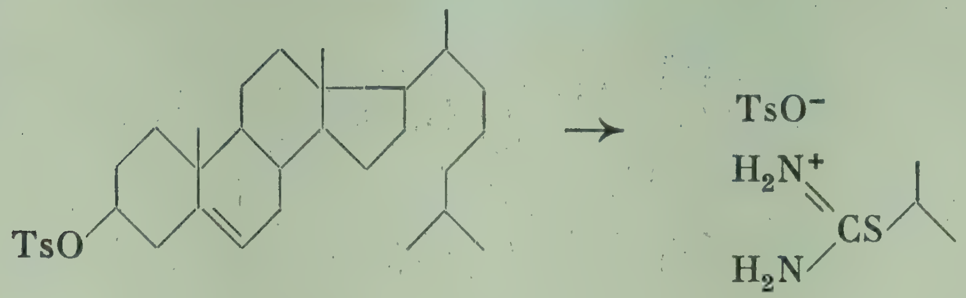
626.



A mixture of 2-benzyloxyquinoline and thiophenol stirred at 150-170° in a dry N_2-atmosphere for 52 hrs. → 2-hydroxyquinoline (Y: 96%) and benzyl phenyl sulfide (Y: 75%). F. e. s. G. Illuminati and H. Gilman, Am. Soc. *71*, 3349 (1949).

Isothioureas from tosylates ←

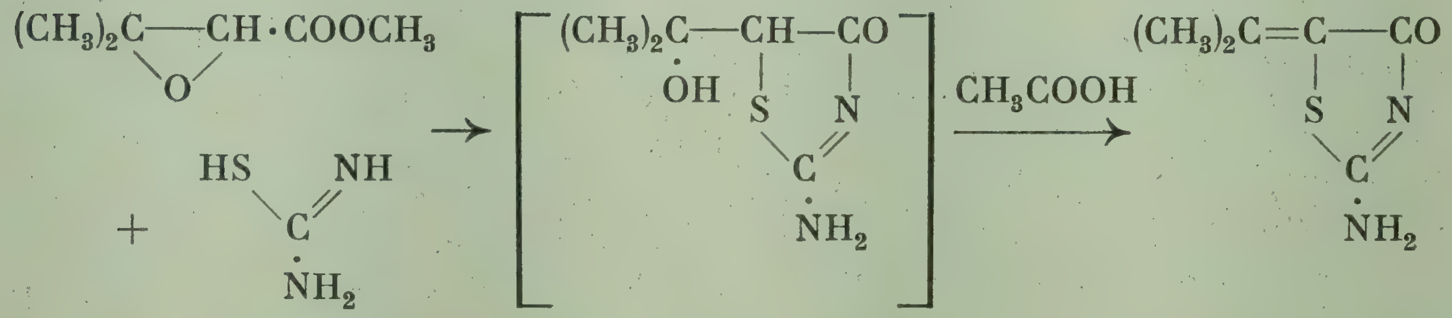
627.



A mixture of 3β-p-toluenesulfonoxy-5-cholestene, thiourea, and 99%-2-propanol refluxed 4 hrs. with addition of water → cholesterylisothiouronium p-toluenesulfonate. Y: 96%. J. W. Ralls, R. M. Dodson, and B. Riegel, Am. Soc. *71*, 3320 (1949).

Thiazolines from glycidic acid esters ○
Dehydration

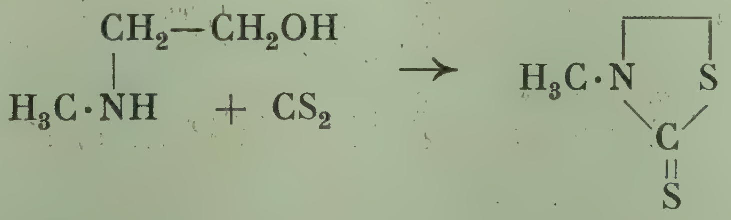
628.



A soln. of methyl dimethylglycidate and thiourea in methanol allowed to stand at 35° for 10 weeks, filtered, evaporated to dryness, and the residue boiled with glacial acetic acid → 2-amino-4-keto-5-isopropylidene-2-thiazoline. Y: 92%. F. e. s. C. C. J. Culvenor et al., Soc. *1949*, 2573.

2-Thiazolidinethiones from aminoalcohols

629.



A soln. of 5 gm. 2-methylaminoethanol in CS_2 heated in a steel autoclave at 120-140° for 3.5 hrs. → 5.8 gm. 3-methyl-2-thiazolidinethione. J. W. Batty and B. C. L. Weedon, Soc. *1949*, 786.

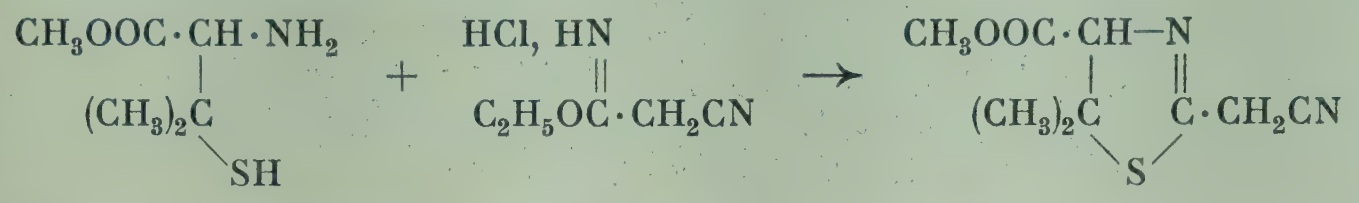
Thiazolidines from cyclic imines ←

s. *6*, 606

Potassium acetate *CH_3COOK*

Thiazolines from iminoesters ○

630.

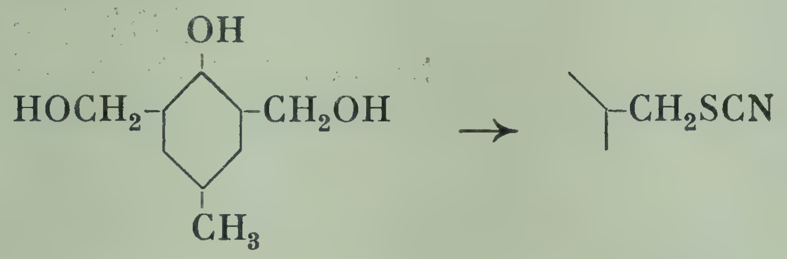


13.8 gm. penicillamine methyl ester hydrochloride, cyanoacetimino ethyl ester hydrochloride, ether, and an aq. K-acetate soln. shaken for 2 hrs. → 13.2 gm. methyl 5,5-dimethyl-2-cyanomethylthiazoline-4-carboxylate. F. e. s. A. H. Cook, G. Harris, and A. L. Levy, Soc. *1949*, 3227.

Potassium thiocyanate *KSCN*

Thiocyanates from alcohols OH → SCN

631.

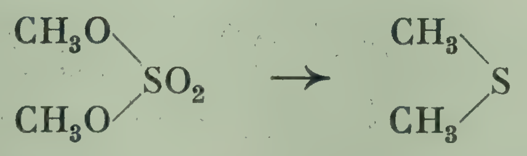


p-Cresoldialcohol and K-thiocyanate in dil. HCl warmed at 70° for 1-2 min. → 2-thiocyanomethyl-4-methyl-6-hydroxymethylphenol. Y: 85%.—Heating for a longer period in addition gives the 2,6-di(thiocyanomethyl) derivative. E. Ziegler and H. Lüdde, M. *79*, 316 (1948).

Sodium sulfide *Na_2S*

Sym. thioethers from sulfuric acid esters ←

632.

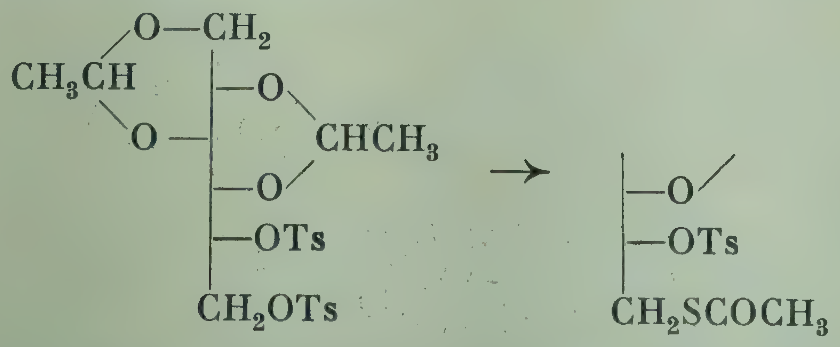


Dimethyl sulfate rapidly dropped into a boiling aq. soln. of Na_2S so that a vigorous reaction takes place and the reaction product distills → dimethyl sulfide. Y: 70%. H. Böhme and W. Krause, Chem. B. *82*, 426 (1949).

Potassium salt *K+*

Thiolic acid esters from tosylates OTs → SCOR

633.

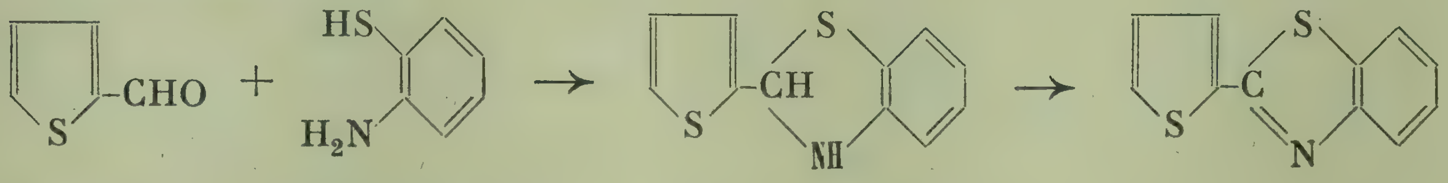


The reaction of prim. p-toluenesulfonates with K-thiolacetate in ethanol or acetone provides a useful method for the preparation of thiolacetates, and, thence, by hydrolysis, of thiols. Sec. p-toluenesulfonates show wide differences in behavior. Methanesulfonates generally react in the same way, but the yields are lower.—E: 5,6-Ditosyl-1,3:2,4-diethylidenesorbitol refluxed 6 hrs. with K-thiolacetate in acetone → 5-tosyl-6-acetyl-1,3:2,4-diethylidene-6-thiosorbitol. Y: 87%. F. e. s. L. N. Owen, J. H. Chapman, and P. Bladon, Soc. *1950*, 579, 585.

Pyridine C_5H_5N

Thiazole ring from o-aminomercaptans via thiazoline ring ○

634.



2-Thiophenealdehyde added in a thin stream to a soln of o-aminothiophenol in pyridine, and stirred 0.5 hr. at 85-95° → crude 2-(2′-thienyl)-benzothiazoline (Y: 92%) dissolved in warm ethanol, a soln. of $FeCl_3$ in ethanol added, and warmed for another 0.5 hr. → 2-(2′-thienyl)-benzothiazole (Y: 74%). W. S. Emerson and T. M. Patrick, Jr., J. Org. Chem. *14*, 790 (1949); method of the thiazoline ring synthesis s. Lankelma and Sharnoff, Am. Soc. *53*, 2654 (1931).

Zinc chloride/sodium sulfate $ZnCl_2/Na_2SO_4$

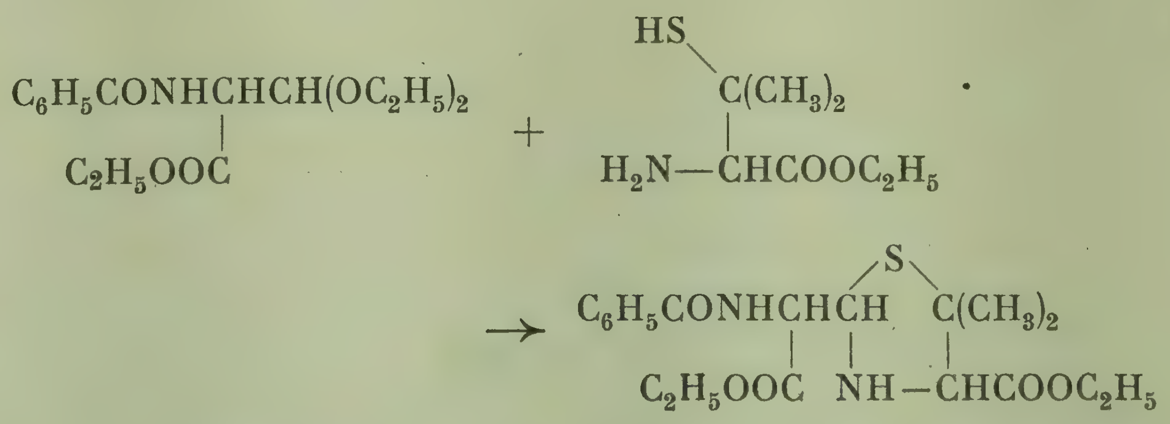
Steroid mercaptals $C(SR)_2$

s. *5*, 430; s. a. D. K. Fukushima, S. Lieberman, and B. Praetz, Am. Soc. *72*, 5205 (1950)

Acetic acid CH_3COOH

Thiazolidines ○

635.



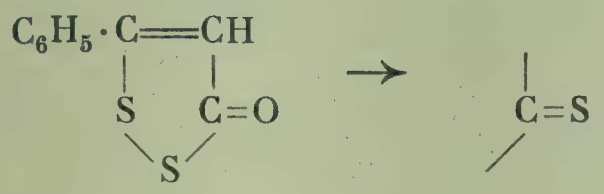
A mixture of DL-penicillamine ethyl ester hydrochloride, ethyl phenylpenaldate diethylacetal, and glacial acetic acid warmed on a steam bath for 30 min. → diethyl DL-phenylpenicilloate. Y: 90%. F. e. s. E. V. Brown, Chemistry of Penicillin *1949*, 528.

Phosphorus pentasulfide *P_2S_5*

Replacement of oxygen by sulfur ←

636. **in N-heterocyclics.** A suspension of *cis*-3-aminocyclohexaneacetic acid lactam (prepn. s. 505) and P_2S_5 in xylene heated with vigorous stirring at 125-130° for 1 hr. in an oil bath → *cis*-3-aminocyclohexaneacetic acid thiolactam (startg. m. f. 124). Y: 77%. M. W. Cronyn, J. Org. Chem. *14*, 1013 (1949); thiohydantoins s. H. C. Carrington and W. S. Waring, Soc. *1950*, 354.

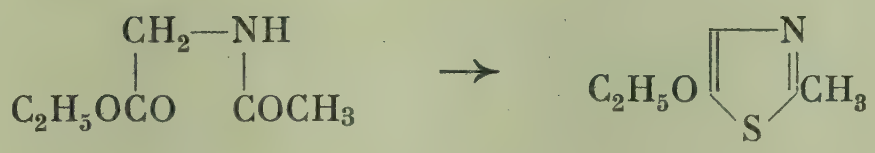
637.



1,2-Dithioles. 5-Oxo-3-phenyl-1,2-dithiole refluxed 7 hrs. with P_2S_5 in CS_2 → 5-thio-3-phenyl-1,2-dithiole. Y: 80%. F. e. s. B. Böttcher and F. Bauer, A. *568*, 227 (1950).

Thiazoles from α-acylaminocarboxylic acid esters ○

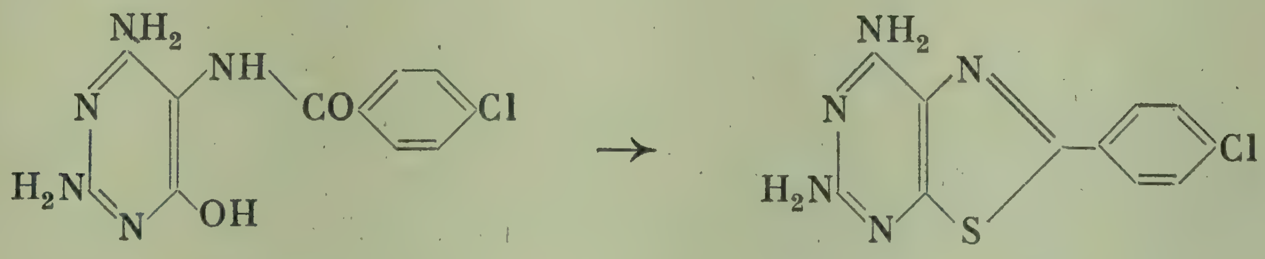
638.



P_2S_5 added in small portions to N-acetylglycine ethyl ester, heated on a steam bath with stirring, chloroform added, when the mixture becomes too viscous to stir, and heating continued for several hrs. after the addition → 2-methyl-5-ethoxythiazole (startg. m. f. HalC⇅H.6794). Y: 65%, isolated as picrate. D. S. Tarbell, H. P. Hirschler, and R. B. Carlin, Am. Soc. *72*, 3138 (1950).

Thiazolo [5.4-d]pyrimidines

639.

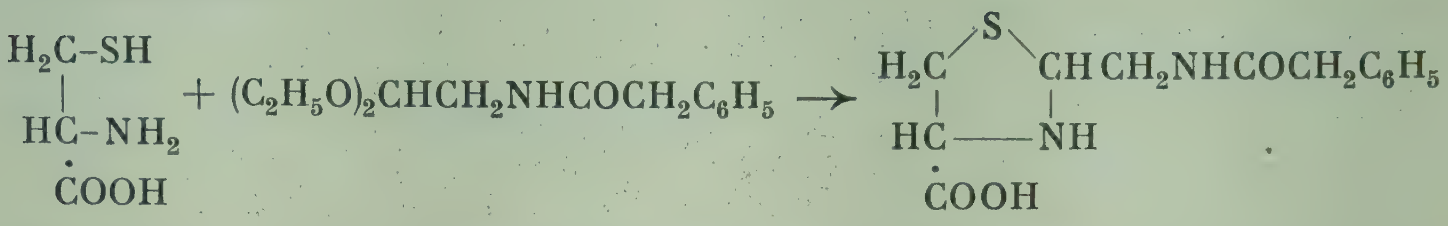


A suspension of 5-(p-chlorobenzamido)-2,4-diamino-6-hydroxypyrimidine and 3 parts of P_2S_5 in tetralin heated with stirring at 150-200° for 2 hrs. → 2-(p-chlorophenyl)-5,7-diaminothiazolo[5.4-d]pyrimidine. Y: 76%. F. e. s. E. A. Falco and G. H. Hitchings, Am. Soc. *72*, 3203 (1950).

Hydrochlorides ←

Thiazolidines

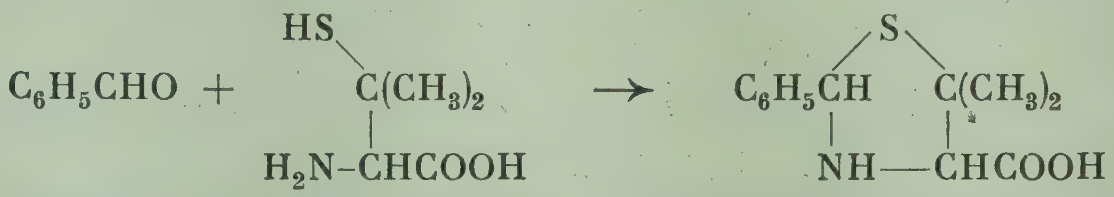
640.



A mixture of phenylacetylaminoacetal and cysteine hydrochloride in water shaken for 1 day, and allowed to stand overnight → 2-(phenylacetylaminomethyl)thiazolidine-4-carboxylic acid. Y: 86% (p. 485). F. e. s. E. V. Brown, Chemistry of Penicillin *1949*, 473.

Hydrofluoric acid *HF*

641.



D-Penicillamine and benzaldehyde in anhydrous dioxane containing HF stirred in a copper flask for 3 hrs. → D-2-phenyl-4-carboxy-5,5-dimethylthiazolidine. Y: 77% (p. 938). F. e. and reactions s. A. H. Cook and I. M. Heilbron, Chemistry of Penicillin *1949*, 921.

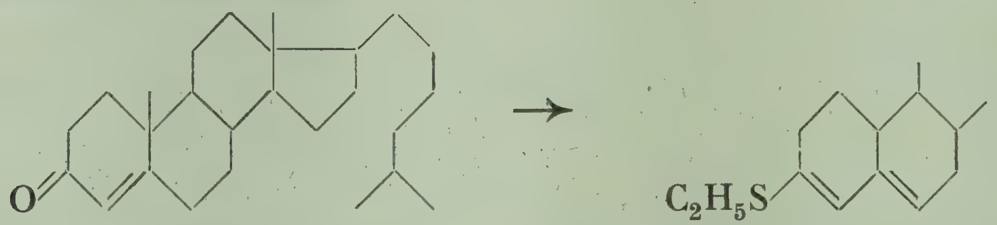
Hydrochloric acid *HCl*

Thioethers from acoxy compounds OAc → SR

s. *6*, 655

Thioenolethers of steroids C:C(SR)

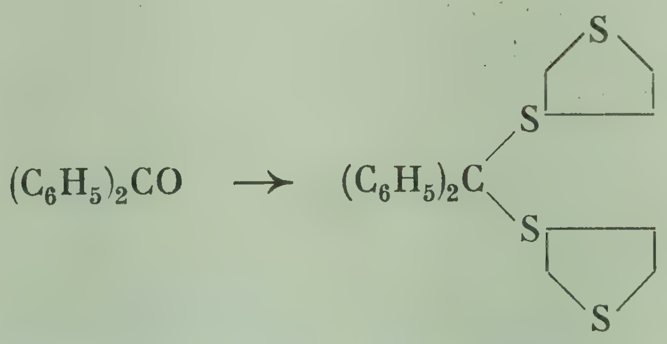
642.



10 drops of concd. HCl added to a mixture of acetic acid, ethyl mercaptan, and cholestenone, then cooled for 0.5 hr. → 3-ethyl-mercapto-3,5-cholestadiene. Y: 78%. J. W. Ralls, R. M. Dodson, and B. Riegel, Am. Soc. *71*, 3320 (1949).

Mercaptals $C(SR)_2$

643.



Anhydrous HCl bubbled through a mixture of benzophenone, 3-thiophenethiol, and xylene at 10-15° for 2 hrs., and kept in a refrigerator overnight → benzophenone di-3-thienyl mercaptal. Y: 80%. F. e. s.

J. W. Brooks, E. G. Howard, and J. J. Wehrle, Am. Soc. *72*, 1289 (1950); also cyclic mercaptals s. H. Hauptmann and B. Wladislaw, Am. Soc. *72*, 707 (1950).

of carbohydrates

s. *1*, 469; s. a. E. Hardegger, E. Schreier, and Z. El Heweihi, Helv. *33*, 1159 (1950)

Nitrogen ↑ SC ⇅ N

Cuprous thiocyanate *CuSCN*

Thiocyanates from amines $NH_2 \rightarrow SCN$

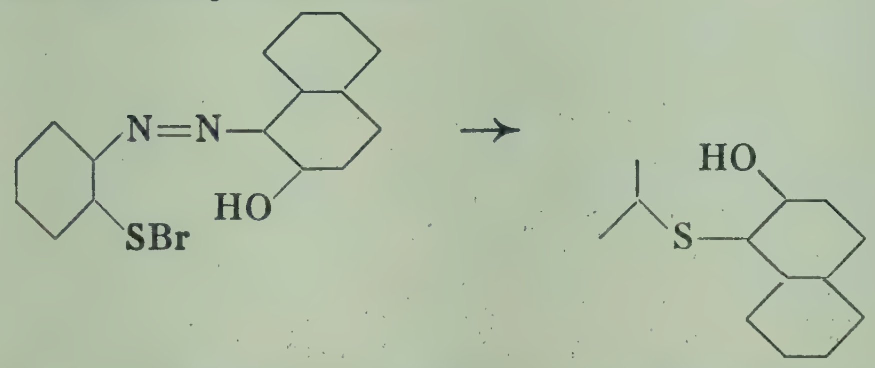
s. *1*, 470; s. a. C. van der Stelt, W. van der Lugt. and W. T. Nauta, R. *70*, 285 (1951)

Halogen ↑ SC ⇅ Hal

Without additional reagents *w.a.r.*

Thioethers from sulfenylbromides SBr → SR

644.



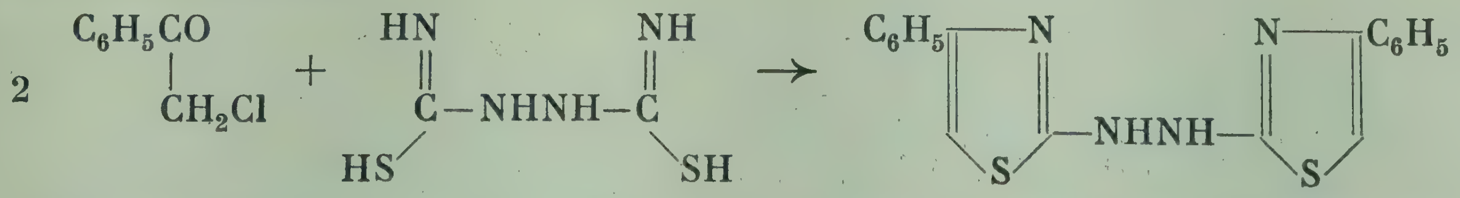
A mixture of o-(2-hydroxy-1-naphthylazo)phenylsulfenyl bromide (prepn. s. 535) and β-naphthol heated at 110-115° for 15 min. → o-(2-hydroxy-1-naphthylazo)phenyl 2-hydroxy-1-naphthyl sulfide. Y: 93%. A. Burawoy and C. Turner, Soc. *1950*, 469; α-ketothioethers s. P. Truitt et al., Am. Soc. *71*, 3511 (1949).

Thiazole ring with thioamides ○

s. *1*, 472/3; *2*, 552-4; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, Am. Soc. *72*, 4526 (1950)

Hydrazothiazoles

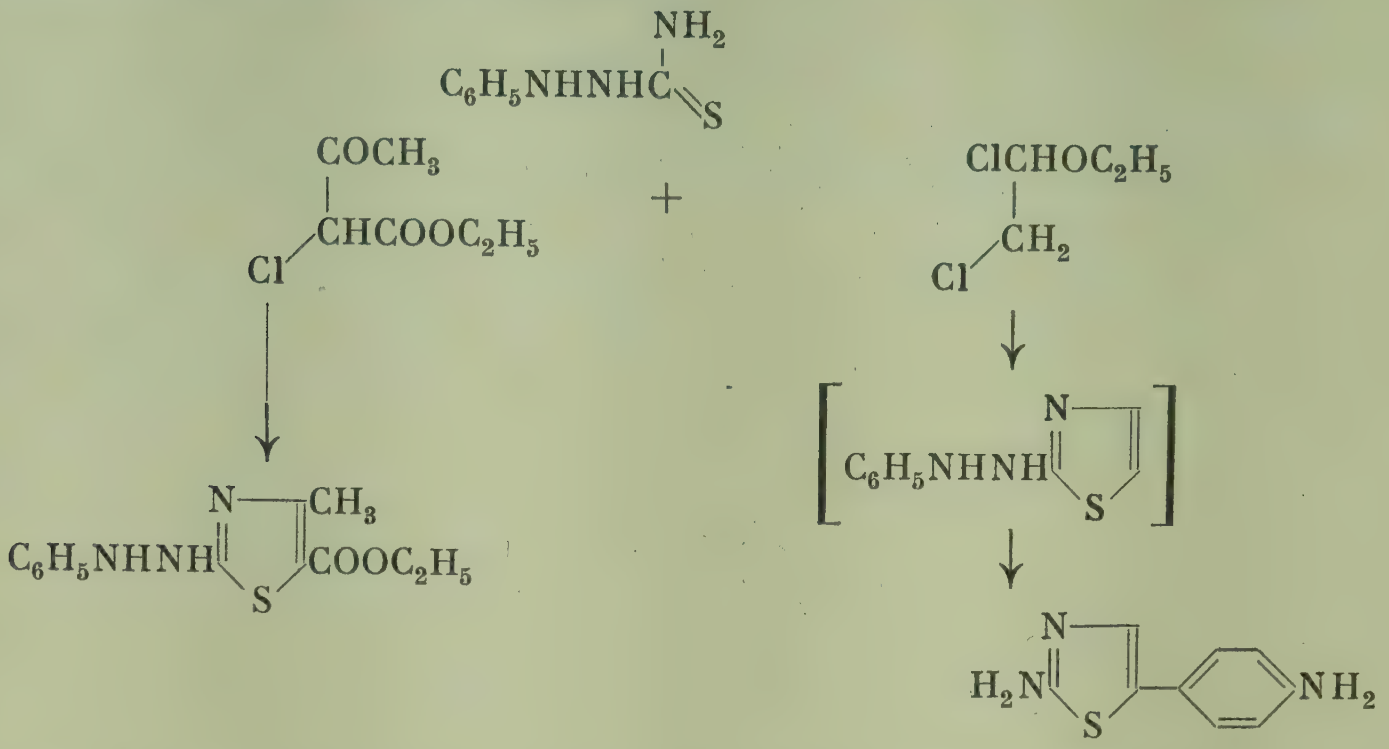
645.



Hydrazine-N,N′-bis(carboxylic acid thioamide) and ω-chloroacetophenone in 96%-alcohol refluxed 0.5 hr. on a water bath → 4,4′-diphenylhydrazothiazole-2,2′. Y: 80%. F. e. s. H. Beyer et al., Chem. B. *82*, 143, 148 (1949).

Thiazoles from thiosemicarbazides, also with benzidine rearrangement

646.


NH₂
C₆H₅NHNHC
S
COCH₃
CHCOOC₂H₅
Cl
+
ClCHOC₂H₅
CH₂
Cl
N
CH₃
C₆H₅NHNH
COOC₂H₅
S
C₆H₅NHNH
N
S
N
H₂N
S
NH₂

1-Phenylthiosemicarbazide in abs. alcohol refluxed 20–30 min. with

α-chloroacetoacetic ester → 2-phenylhydrazino-4-methyl-5-carbethoxythiazole. Y: almost 100%.	α,β-dichloroether → 2-amino-5-(p-aminophenyl)thiazole dihydrochloride. Y: almost 100%.

F. e. s. H. Beyer and G. Henseke, B. *83*, 247 (1950).

Sodium hydroxide *NaOH*

Sulfones $R \cdot SO_2 \cdot R$

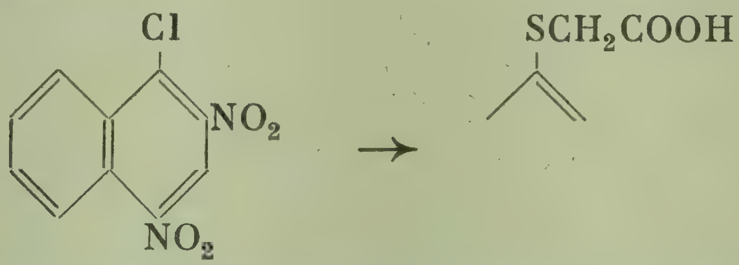
Sulfonylcarboxylic acids

s. *2*, 556; cf. C. S. Marvel, R. S. Johnson, and N. A. Meinhardt, J. Org. Chem. *13*, 822 (1948); Am. Soc. *73*, 859 (1951)

Sodium hydrogen carbonate *$NaHCO_3$*

Thioethers from halides Hal → SR

647.


Cl
NO₂
NO₂
SCH₂COOH

A soln. of thioglycolic acid in a little alcohol, then $NaHCO_3$ added to a boiling suspension of 1-chloro-2,4-dinitronaphthalene in alcohol, stirred and boiled until dissolved → (2,4-dinitro-1-naphthyl)mercaptoacetic acid (startg. m. f. 889). Y: 60%.—Temp. and pH are very important, and if not correct, 2,4-dinitro-1-naphthol is chiefly obtained. G. Leandri, G. *79*, 50 (1949); α-ketothioethers s. S. Teich and D. Y. Curtin, Am. Soc. *72*, 2481 (1950).

Sodium sulfide *Na_2S*

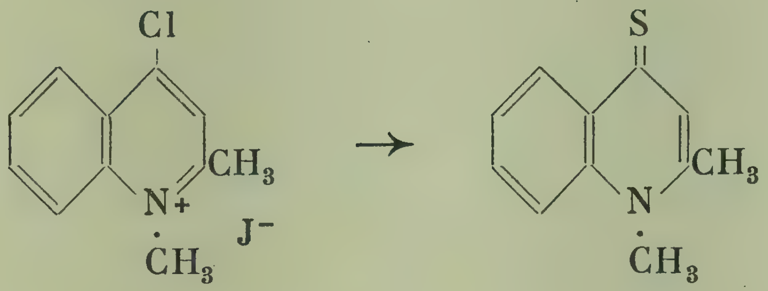
Sym. thioethers from halides 2 RHal → RSR

s. *5*, 442; s. a. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, Am. Soc. *72*, 2856 (1950)

Sodium hydrogen sulfide *NaHS*

Tert. amines from quaternary ammonium salts with simultaneous replacement of chlorine by sulfur ←

648.



A mixture of 4-chloroquinaldine methiodide and NaHS (containing 28% water of crystallization) in ethanol refluxed 12 hrs. → N-methyl-4-thioquinaldone. Y: 83%.—The nature of the substituent in position 2 has a definite influence, both on the synthesis and the properties of the thiones, depending upon the electron-attracting or -releasing character of the group. F. e. s. E. Campaigne, R. E. Cline, and C. E. Kaslow, J. Org. Chem. *15*, 600 (1950).

Sodium sulfite *Na_2SO_3*

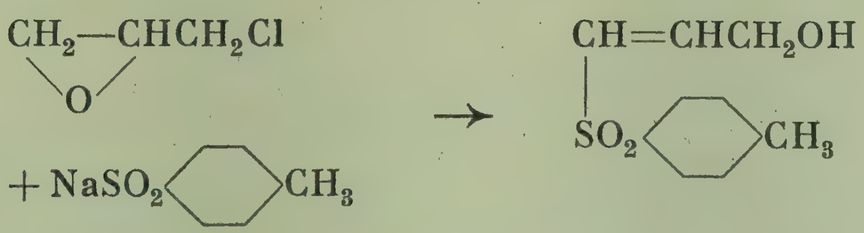
Sulfonic acids Hal → SO_3H

s. *1*, 488/9; *3*, 523; s. a. P. Petitcolas and R. Sureau, Bl. *1950*, 466

Sodium salt *Na^+*

Hydroxyethylenesulfones from oxidohalides ←

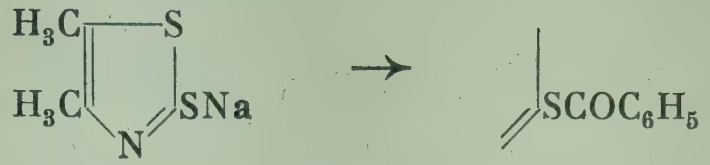
649.



Epichlorohydrin and Na-p-toluenesulfinate in water-alcohol kept at 32° for 24 hrs. → 3-p-toluenesulfonyl-2-propen-1-ol. Y: 90%. F. e. s. C. C. J. Culvenor, W. Davies, and W. E. Savige, Soc. *1949*, 2198.

Thiolic acid esters from carboxylic acid chlorides COCl → COSR

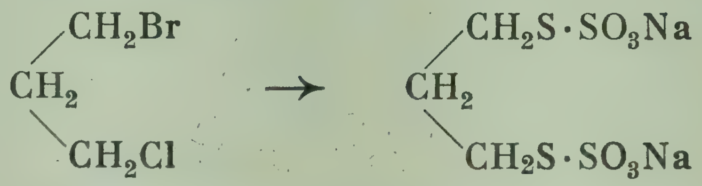
650.



Benzoyl chloride added to a suspension of Na-4,5-dimethylthiazole-2-mercaptide in benzene, and the soln. formed refluxed for 1 hr. → 4,5-dimethyl-2-benzoylmercaptothiazole. Y: 99%. F. e. s. F. D. Stewart and R. A. Mathes, J. Org. Chem. *14*, 1111 (1949).

Alkylthiosulfates from halides Hal → SSO_3^-

651.

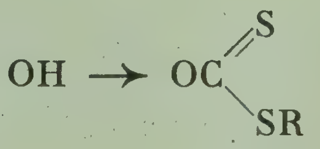


1-Chloro-3-bromopropane added with stirring to aq. Na-thiosulfate, stirring continued at 40-45° for 60-80 hrs. → Na trimethylene dithiosulfate (startg. m. f. 659). Y: 86%. F. e. s. Ya. G. Mazover, Ж. *19*, 843, 849 (1949); C. A. *44*, 3436a, f; s. a. U. Weiss and S. Sokol, Am. Soc. *72*, 1687 (1950).

Potassium salt *K^+*

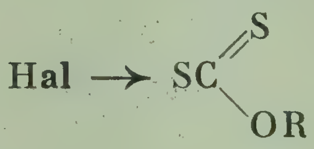
Xanthates

from alcohols
s. *6*, 841



$OH \rightarrow OC(=S)SR$

from halides
s. *6*, 656



$Hal \rightarrow SC(=S)OR$

Ammonia *NH_3*

Thioethers from halides Hal → SR

652. A slow stream of NH_3 introduced at ca. 50° for 30 min. into a mixture of p-nitrobenzyl chloride and benzylmercaptan in abs. alcohol → p-nitrobenzyl benzyl sulfide. Y: 95%. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, Am. Soc. *72*, 2856 (1950).

Alumina *Al_2O_3*

Mercaptans from halides Hal → SH

653. $(C_6H_5)_3C\cdot Cl \rightarrow (C_6H_5)_3C\cdot SH$

Dry H_2S passed into a mixture of triphenylmethyl chloride and activated Al_2O_3 (Alcoa F-20) in dry dioxane for 15 hrs. at such a rate as to agitate the suspended Al_2O_3 gently and to keep the soln. saturated with the gas → triphenylmethyl mercaptan. Y: 75-80%. N. Kharasch and H. R. Williams, Am. Soc. *72*, 1843 (1950).

Ammonium thiocyanate *NH_4SCN*

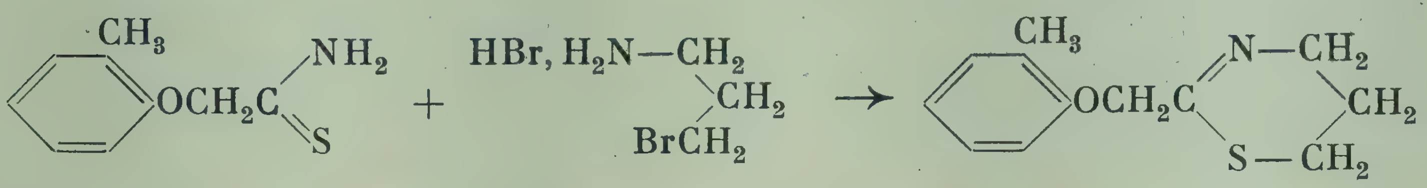
Thiocyanates from chlorides Cl → SCN

s. *5*, 448; s. a. E. Szarvasi, Bl. *1950*, 463

Hydrobromides ←

1,3-S,N-Heterocyclics ○
1,3-Thiazines

654.

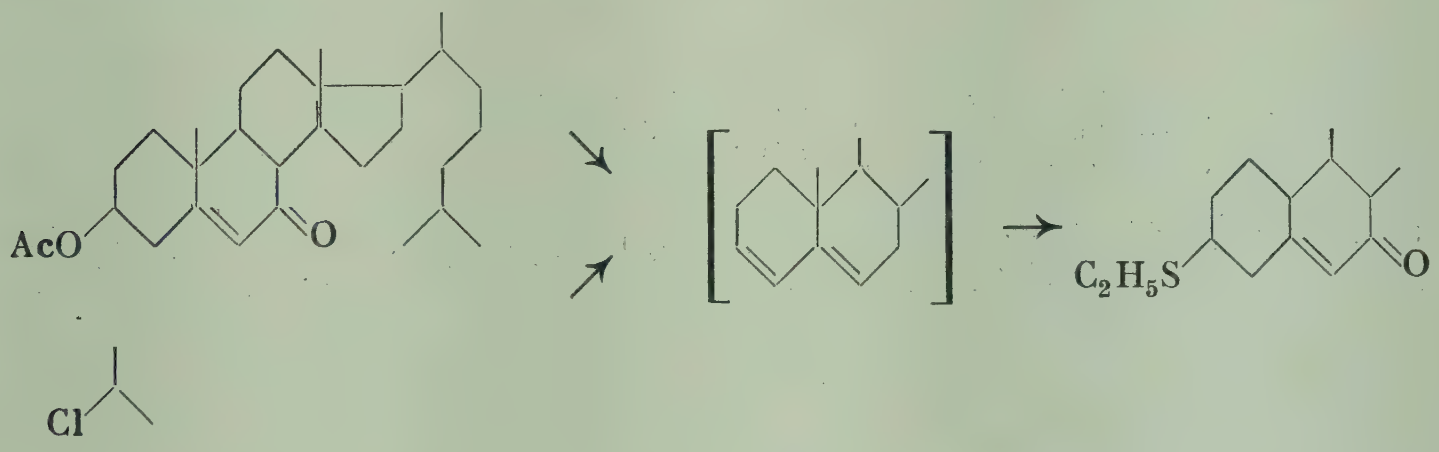


o-Toloxyacetothiamide and 3-bromopropylamine hydrobromide heated 5 min. at 160° → 2-(o-toloxymethyl)penthiazoline. Y: 69%. F. e. s. C. Djerassi and C. R. Scholz, J. Org. Chem. *15*, 694 (1950).

Hydrochloric acid *HCl*

Thioethers from acoxy compounds and chlorides ←
1,6-Addition

655.



Ethylmercaptan added to a soln. of 7-ketocholesteryl acetate or 3β-chloro-5-cholesten-7-one in glacial acetic acid containing concd. HCl, and worked up after 30 min. → 3-ethylmercapto-5-cholesten-7-one. Y: 83% and 80% respectively. J. W. Ralls, R. M. Dodson, and B. Riegel, Am. Soc. *71*, 3320 (1949).

Via intermediates *v.i.*

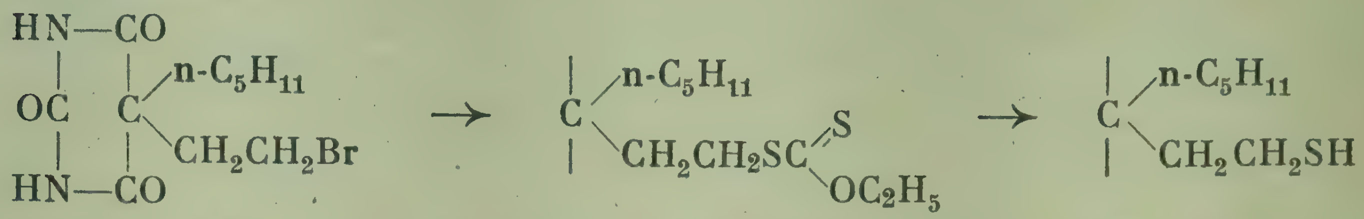
Mercaptans from halides Hal → SH

via isothioureas

s. *1*, 493-5; mercaptopyrimidines s. M. Polonovski and H. Schmitt, Bl. *1950*, 616

via xanthates

656.



A soln. of 5-n-amyl-5-β-bromoethylbarbituric acid and freshly prepared K-ethylxanthate in abs. alcohol kept 5 hrs. at ca. 45° → crude 5-n-amyl-5-(β-ethylxanthoethyl)barbituric acid (Y: 85%) dissolved in 10%-NaOH, aq. NH_3 added with stirring, and allowed to stand at room temp. for 7 hrs. → 5-n-amyl-5-β-mercaptoethylbarbituric acid (Y: 79%). F. e. s. G. S. Skinner and J. B. Bicking, Am. Soc. *72*, 1140 (1950).

Carboxymethylthioethers from halides Hal → SCH_2COOH

657. $n\text{-}C_4H_9Br \rightarrow [n\text{-}C_4H_9SH] + ClCH_2COOH \rightarrow n\text{-}C_4H_9SCH_2COOH$

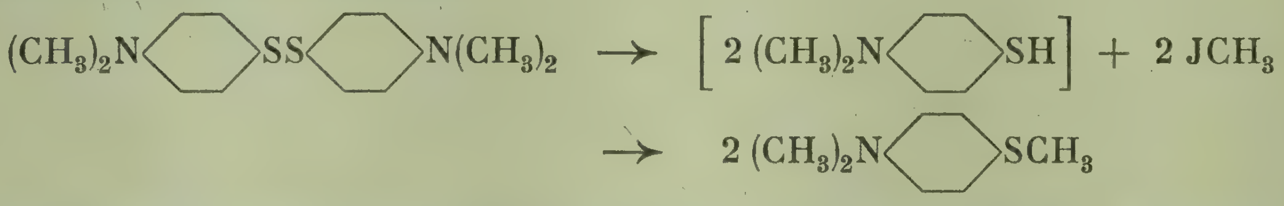
A soln. of thiourea in 95%-alcohol refluxed 4 hrs. with n-butyl bromide, most of the alcohol distilled off, aq. NaOH added, refluxing continued for an additional 2 hrs., more aq. NaOH added until the mercaptan which has separated is dissolved, cooled to ca. 0°, neutral aq. Na-chloroacetate added, allowed to warm to room temp., finally refluxed 1 hr. → n-butylthioacetic acid. Y: 90%. S. Chodroff and W. F. Whitmore, Am. Soc. *72*, 1073 (1950).

Sulfur ↑ SC ⇅ S

Sodium/liq. ammonia *Na/NH₃*

Thioethers from disulfides ←

658.

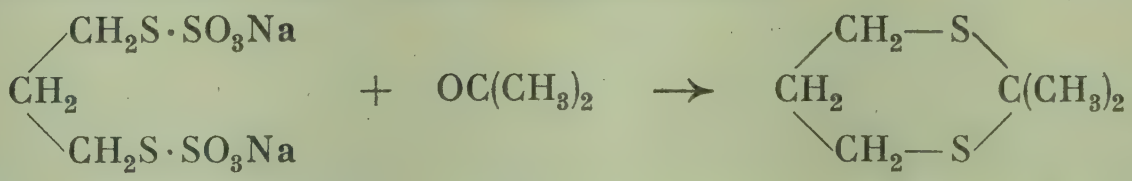


Bis-(p-dimethylaminophenyl) disulfide added slowly with stirring to a soln. of Na in liq. NH_3 until the color of the soln. has turned from blue to pink, then methyl iodide added dropwise → p-dimethylaminophenyl methyl sulfide. Y: 79%. H. Gilman and F. J. Webb, Am. Soc. *71*, 4062 (1949).

Hydrochloric acid *HCl*

Cyclic mercaptals from alkyldi(thiosulfates) ○

659.



15%-alc. HCl added with cooling and frequent shaking to Na trimethylene dithiosulfate (prepn. s. 651) and acetone over a period of

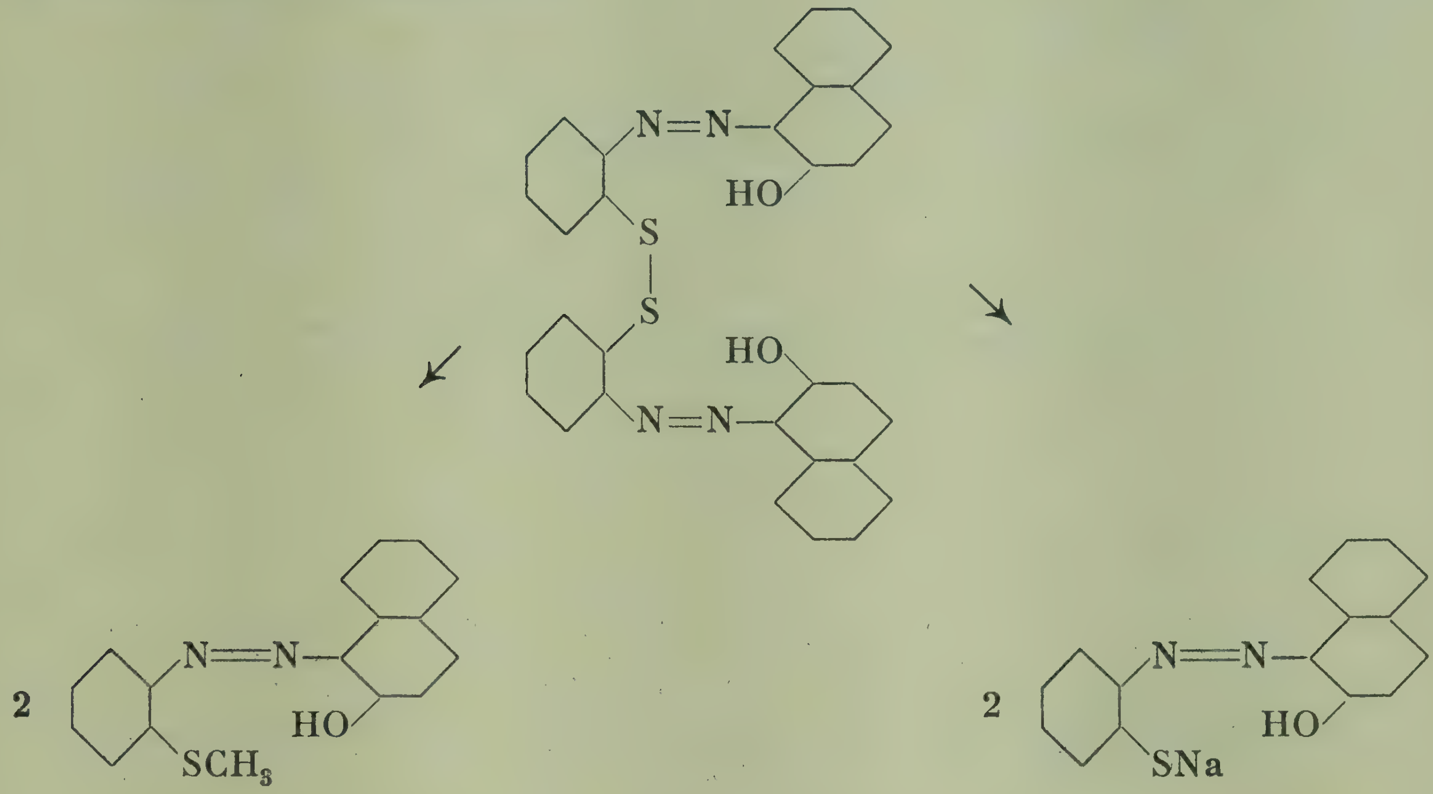
6 hrs., then allowed to stand overnight → acetone trimethylene mercaptal. Y: 58%. F. e. s. Ya. G. Mazover, Ж. *19*, 843, 849 (1949); C. A. 44, 3436a, f.

Via intermediates *v.i.*

Thioethers and mercaptans from disulfides ←

o-Mercaptoazo compounds

660.



A suspension of di-o,o′- (2-hydroxy-1-naphtylazo) phenyl disulfide

in methanol shaken 2 hrs. at room temp. with aq. Na_2S, water added followed by 4 additions of aq. NaOH and dimethyl sulfate with vigorous shaking → 1-(o-methylmercaptophenylazo)-2-naphthol. Y: ca. 100%.

in ethanol shaken 4 hrs. at room temp. with aq. Na_2S, then water added → Na salt of 1-(o-mercaptophenylazo)-2-naphthol. Y: 88%.

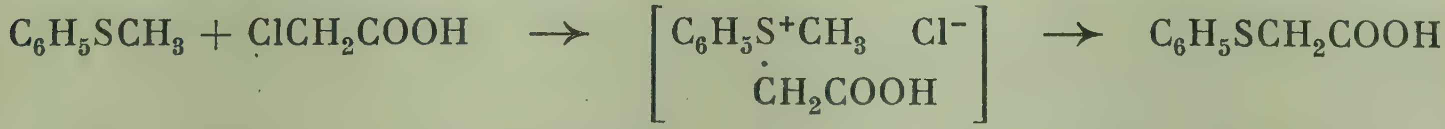
A. Burawoy and C. Turner, Soc. *1950*, 469.

Carbon ↑ SC ⇅ C

Without additional reagents *w.a.r.*

Transetherification of thioethers SR → SR′

661.



$$C_6H_5SCH_3 + ClCH_2COOH \rightarrow \left[\begin{array}{l} C_6H_5\overset{}{S}^+CH_3 \quad Cl^- \\ \quad CH_2COOH \end{array}\right] \rightarrow C_6H_5SCH_2COOH$$

A mixture of thioanisol and 3-4 parts of chloroacetic acid heated 8-10 hrs. in a boiling water bath → phenylthioglycolic acid. Y: ca. 80%. F. e. s. F. Krollpfeiffer et al., A. *566*, 139 (1950); B. *83*, 90 (1950).

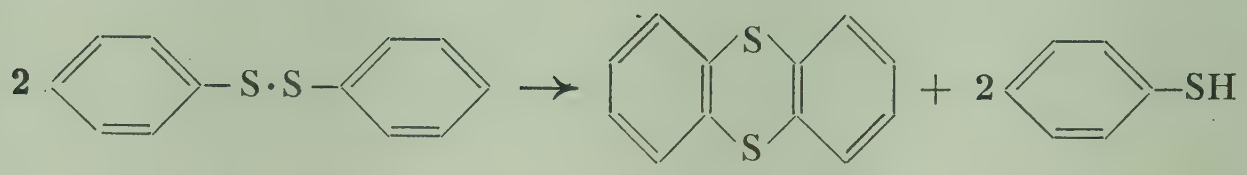
Elimination

Hydrogen ↑ SC ⇑ H

Without additional reagents *w.a.r.*

Thianthrenes from disulfides ○
Disproportionation

662.



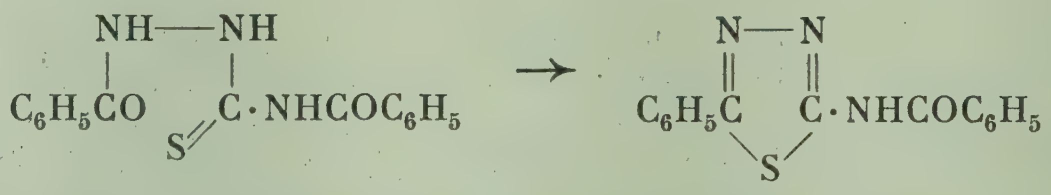
Diphenyl disulfide heated in a CO_2-atmosphere at 270° for 6 hrs. → thianthrene. Y: 60%. A. Schönberg and A. Mustafa, Soc. *1949*, 889.

Oxygen ↑ SC ⇑ O

Phosphoric acid *H_3PO_4*

1,3,4-Thiadiazoles from acylthiosemicarbazides ○

663.

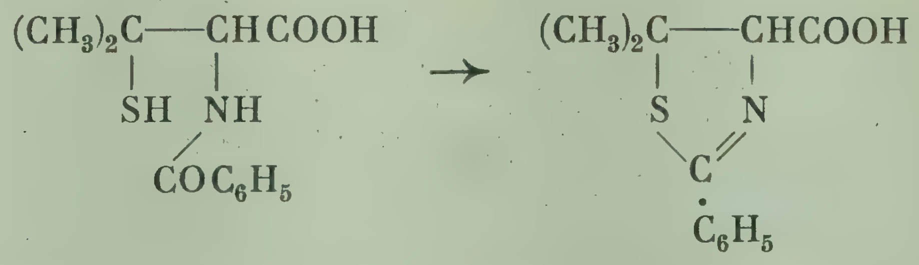


3 gm. 1,4-dibenzoylthiosemicarbazide allowed to react with syrupy H_3PO_4 at 120° → 2.4 gm. 2-benzamido-5-phenyl-1,3,4-thiadiazole. F. e. s. E. Hoggarth, Soc. *1949*, 1163.

Hydrochloric acid *HCl*

Thiazolines

664.

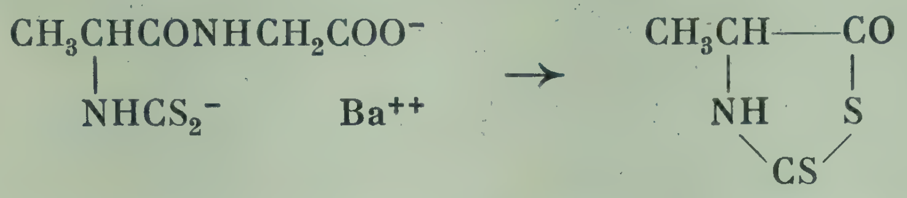


N-Benzoylpenicillamine refluxed with dil. HCl under N_2 for 16 hrs. → 2-phenyl-4-carboxy-5,5-dimethylthiazoline. Y: 91% (p. 471). F. e. s. H. M. Crooks, Jr., Chemistry of Penicillin *1949*, 455.

Nitrogen ↑ **SC ⇑ N**

Hydrochloric acid *HCl*

Thiazolidones ○
Elimination of terminal moieties from peptides

665.


Ba-(N-dithiocarboxyalanyl)glycine in water acidified with *N* HCl → 2-thio-4-methylthiazolid-5-one. Y: 75%. F. e. s. A. L. Levy, Soc. *1950*, 404.

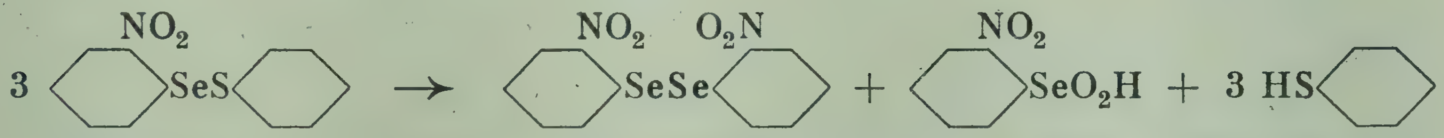
Formation of Rem—Rem Bond

Exchange

Sulfur ↑ **RemRem ⇅ S**

Potassium hydroxide *KOH*

Diselenides from selenylsulfides ←

666.


o-Nitrobenzeneselenyl phenyl sulfide (prepn. s. 602) refluxed with aq.-alc. (1 : 1) KOH until the soln. is almost colorless → o,o′-dinitrodiphenyl diselenide (Y: 97.8%) o-nitrobenzeneseleninic acid (Y: 87.2%), and thiophenol (Y: 90.8%). H. Reinboldt and E. Giesbrecht, A. *568*, 198 (1950).

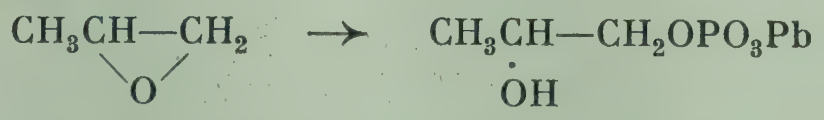
Formation of Rem—C Bond

Uptake

Addition to Oxygen and Carbon **RemC ⇓ OC**

Potassium salt *K+*

Phosphoric acid esters from oxido compounds ←

667.


Propylene oxide and K_2HPO_4 in water heated 12 hrs. in a pressure bottle on a steam bath, and the reaction product isolated as Pb-salt →

Pb-propane-1,2-diol-α-phosphate. Y: 87%.—This procedure is especially adaptable to syntheses involving radioactive phosphorus. G. P. L. Lampson and H. A. Lardy, J. Biol. Chem. *181*, 697 (1949); f. e. s. *181*, 693.

Addition to Carbon RemC ⇓ CC

Without additional reagents *w.a.r.*

Organo mercury compounds from ethylene derivatives $C{:}C \rightarrow C(HgOCOCH_3)\cdot C(OCH_3)$

s. *1*, 498-500; s. a. G. A. Wiese and J. W. Jones, J. Am. Pharm. Assoc. *39*, 286 (1950); D. E. Pearson, M. V. Sigal, Jr., and R. H. Krug, J. Org. Chem. *15*, 1048, 1055 (1950)

Acyl peroxides *$(RCOO)_2$*

Silanes from ethylene derivatives ←

s. *3*, 534; with benzoyl peroxide s. G. N. Gadsby, Research *3*, 338 (1950)

Exchange

Hydrogen ↑ RemC ⇅ H

Lithium *Li*

Silanes ⋮SiH → ⋮SiR

s. *3*, 535; s. a. H. Gilman and H. W. Melvin, Jr., Am. Soc. *71*, 4050 (1949); influence of the solvent s. W. H. Nebergall, Am. Soc. *72*, 4702 (1950)

Organo tin compounds ⋮SnH → ⋮SnR

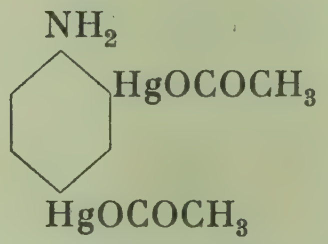
668. $(C_6H_5)_3SnH + LiC_6H_5 \rightarrow (C_6H_5)_4Sn$

Triphenyltin hydride treated with phenyl-Li, then benzyl chloride added to react with any triphenyltinlithium that might have been formed → tetraphenyltin. Y: 91%. G. Gilman and H. W. Melvin, Jr., Am. Soc. *71*, 4050 (1949).

Sodium hydrogen carbonate *$NaHCO_3$*

Mercuration $H \rightarrow Hg^+$

669.



Aniline added with stirring at pH 4.25 to a mixture of glacial acetic acid, $NaHCO_3$, and mercuric acetate → 2,4-diacetoxymercurianiline. Y: 93.5%.—Careful adjustment of the pH is essential for obtaining high yields. T. C. Bruice, Am. Soc. *72*, 1398 (1950).

Oxygen ↑ RemC ⇅ O

Magnesium *Mg*

Arsonium salts from arsine oxides ←

670. $$\begin{tikzcd}(C_6H_5)_3AsO + C_6H_5MgBr \arrow[r] & {[(C_6H_5)_4AsOMgBr} \arrow[r] & (C_6H_5)_4AsBr] \arrow[d, "HCl"] \\ & & (C_6H_5)_4AsCl, HCl\end{tikzcd}$$

Phenyl-MgBr from bromobenzene and Mg in ether added with vigorous stirring to a soln. of triphenylarsine oxide (prepn. s. 153) in hot benzene, stirring continued for 15 min., then refluxed and stirred for 30 min., the addition product hydrolyzed with dil. HCl, and crystallized from concd. HCl → tetraphenylarsonium chloride hydrochloride. Y: 74-80%. R. L. Shriner and C. N. Wolf, Org. Synth. *30*, 95 (1950).

Nitrogen ↑ RemC ⇅ N

Cuprous oxide *Cu_2O*

Cyanoarsines from hydrazines via chloroarsines ←

671. $$2\ C_6H_5NHNH_2 + H_3AsO_4 + HCl \longrightarrow (C_6H_5)_2AsCl \longrightarrow (C_6H_5)_2AsCN$$

Phenylhydrazine added slowly with stirring at 75° to a mixture of 25% excess technical grade arsenic acid and Cu_2O, extracted with CCl_4, and the extract shaken with concd. HCl → crude diphenylchloroarsine (Y of pure product 69-73%) treated during 0.5 hr. with ca. 10% excess of aq. 33%-NaCN at 60° with stirring, which is continued at the same temp. for 0.5 hr. → diphenylcyanoarsine (Y: ca. 85%; purity 87%). Overall Y: 60%. R. L. Barker et al., J. Soc. Chem. Ind. *68*, 277 (1949).

Halogen ↑ RemC ⇅ Hal

Without additional reagents *w.a.r.*

Phosphonic acid esters from phosphites
Arbusov rearrangement ←

s. *4*, 597; s. a. F. W. Mitchell, Jr., and H. J. Lucas, Am. Soc. *72*, 5779 (1950); A. H. Ford-Moore and B. J. Perry, Org. Synth. *31*, 33 (1951)

Lithium *Li*

Silanes ←

s. *3*, 542; s. a. H. Gilman and G. N. R. Smart, J. Org. Chem. *15*, 720 (1950)

Organo lead compounds ←·

672. $PbJ_2 + 3\,CH_3Li + CH_3J \rightarrow (CH_3)_4Pb \rightarrow (CH_3)_2PbBr_2$

A soln. of methyl-Li in ether added during 20 min. to a suspension of PbI_2 in ether containing methyl iodide → ethereal soln. of tetramethyl-Pb (Y: ca. 100%) washed with dil. HCl and water, dried, cooled to —60°, and a soln. of Br in chloroform added with stirring → dimethyl-Pb-dibromide (Y: 92%). H. Gilman and R. G. Jones, Am. Soc. *72*, 1760 (1950).

Sodium *Na*

Tert. arsines AsR_3

673. $3\,C_6H_5Cl + AsCl_3 \rightarrow (C_6H_5)_3As$

A mixture of $AsCl_3$ and chlorobenzene added dropwise with stirring over a period of 1.5-2 hrs. to powdered Na covered with benzene and heated on a steam bath, which is removed when the reaction mixture begins to boil, then stirred and refluxed 12 hrs. → triphenylarsine (startg. m. f. 153). Y: 88-97%. R. L. Shriner and C. N. Wolf, Org. Synth. *30*, 95 (1950).

Sodium cyanide *NaCN*

Cyanoarsines from chloroarsines AsCl → AsCN

s. *6*, 671

Sodium salt *Na+*

Phosphonic acid esters from phosphites

s. *4*, 604; s. a. B. A. Arbusov and B. P. Lugovkin, Ж. *21*, 99 (1951); C. A. *45*, 7002e

Potassium salt *K+*

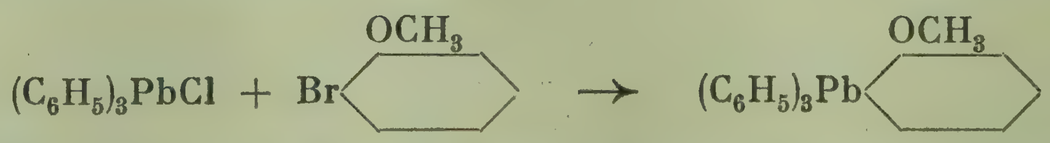
Selenocyanates from halides Hal → SeCN

s. *3*, 544; s. a. H. Reinboldt and H. Vieira de Campos, Am. Soc. *72*, 2784 (1950)

Magnesium *Mg*

Organo lead compounds ⁝PbH → ⁝PbR

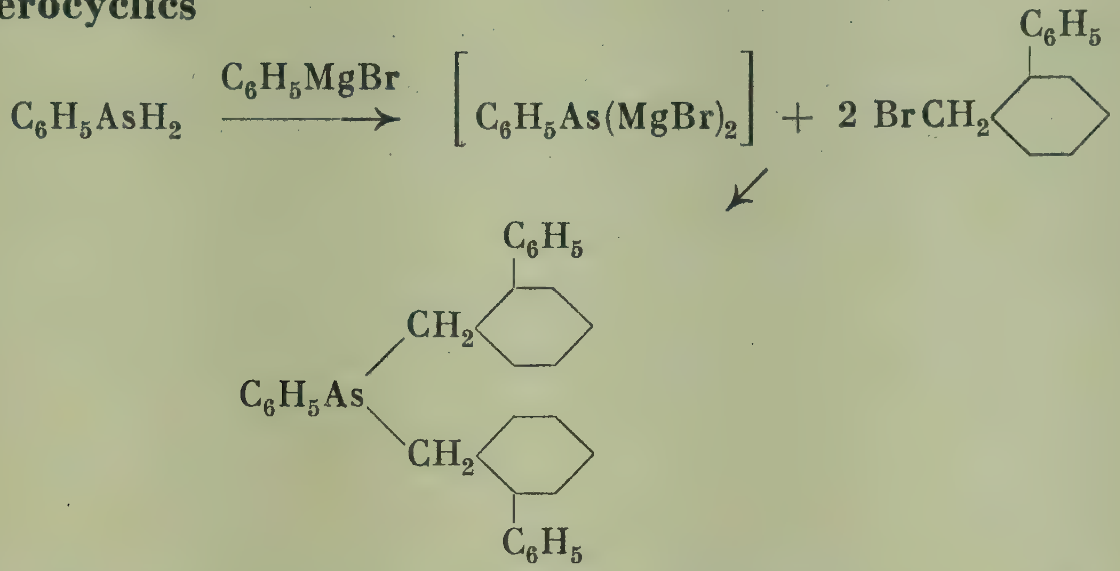
674.



Triphenyllead chloride (prepn. s. 545) added to o-anisyl-MgBr (from o-bromoanisole and Mg in ether), diluted with ether and toluene after an initial brief period of vigorous refluxing, and heating continued under reflux for 1 hr. → (o-anisyl)triphenyllead. Y: 81%. F. e. s. H. Gilman and D. S. Melstrom, Am. Soc. *72*, 2953 (1950).

Arsines via arsenic magnesium compounds ←
As-Heterocyclics

675.



A soln. of phenylarsine in benzene added with cooling to phenyl-MgBr, from bromobenzene and Mg in ether, refluxed 30 min., cooled, a soln. of o-phenylbenzyl bromide in benzene added during 20 min., refluxed 1 hr., cooled, and hydrolyzed with aq. NH_4Cl → phenylbis-(o-phenylbenzyl)arsine. Crude Y: 94%. G. H. Cookson and F. G. Mann, Soc. *1949*, 2888; As-heterocyclics s. Soc. *1950*, 1917, 1923.

Remaining Elements ↑ RemC ↓↑ Rem

Zinc oxide *ZnO*

Chloroarsines ←

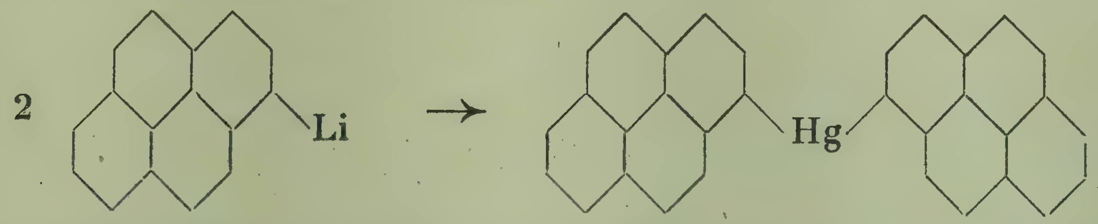
676. $$C_6H_5AsCl_2 + 3\ C_6H_5AsO \rightarrow 2\,(C_6H_5)_2AsCl + As_2O_3$$

ZnO added in small portions to a 3 : 1 mixture of phenyldichloroarsine (prepn. s. 542) and phenylarsenoxide, placed in a mild steel flask, with stirring at 60°, then the temp. raised rapidly to 120°, and maintained at this temp. with stirring for 2.5 hrs. → diphenylchloroarsine. Y: 93.6%. R. L. Barker et al., J. Soc. Chem. Ind. *68*, 295 (1949).

Mercuric chloride *$HgCl_2$*

Diaryl mercury from aryl lithium ←

677.



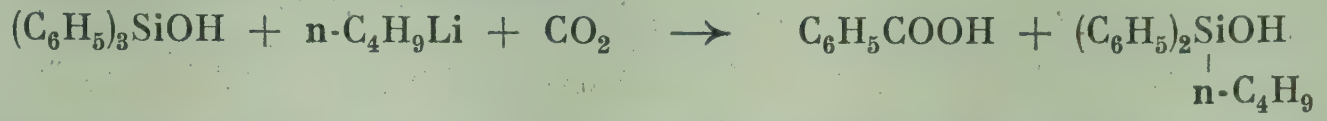
Finely powdered $HgCl_2$ added to an ethereal suspension of 3-pyrenyl-Li, and shaken for 12 hrs. after the initial vigorous reaction subsides → di-3-pyrenyl-Hg. Y: 80.4%. A. Berg, Acta Chem. Scand. *3*, 655 (1949).

Carbon ↑ **RemC ⇅ C**

Lithium *Li*

Cleavage of silanes and silanols ←

678.



$$(C_6H_5)_3SiOH + n\text{-}C_4H_9Li + CO_2 \rightarrow C_6H_5COOH + (C_6H_5)_2\underset{\text{n-}C_4H_9}{\underset{|}{Si}}OH$$

An ethereal soln. of n-butyl-Li added slowly with vigorous agitation to an ethereal soln. of triphenylsilanol in an atmosphere of dry N_2, refluxed 24 hrs., and poured on crushed Dry Ice → benzoic acid (Y: 76%) and diphenyl-n-butylsilanol (Y: 86%).—n-Butyl-Li attacks the C-Si bond rather than the C-H bond as in triphenylcarbinol where metalation of the ar. nucleus occurs. F. e. and limitations s. H. Gilman, R. A. Benkeser, and G. E. Dunn, Am. Soc. *72*, 1689 (1950).

Formation of C—C Bond

Uptake

Addition to Hydrogen and Carbon CC ⇓ HC

Potassium amide *KNH_2*

Carboxylic acids from hydrocarbons H → COOH
Synthesis with addition of 1 C-atom

s. *4*, 614; s. a. Am. Soc. *72*, 3290 (1950); M. C. Kloetzel and H. E. Mertel, Am. Soc. *72*, 4786 (1950)

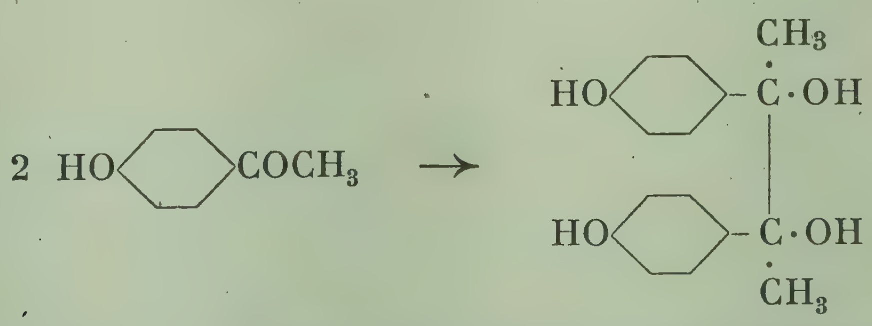
Kolbe synthesis of phenolcarboxylic acids from phenols
s. *4*, 615; s. a. M. *81*, 1071 (1950)

Addition to Oxygen and Carbon CC ⇓ OC

Electrolysis ↯

Pinacols ←

679.



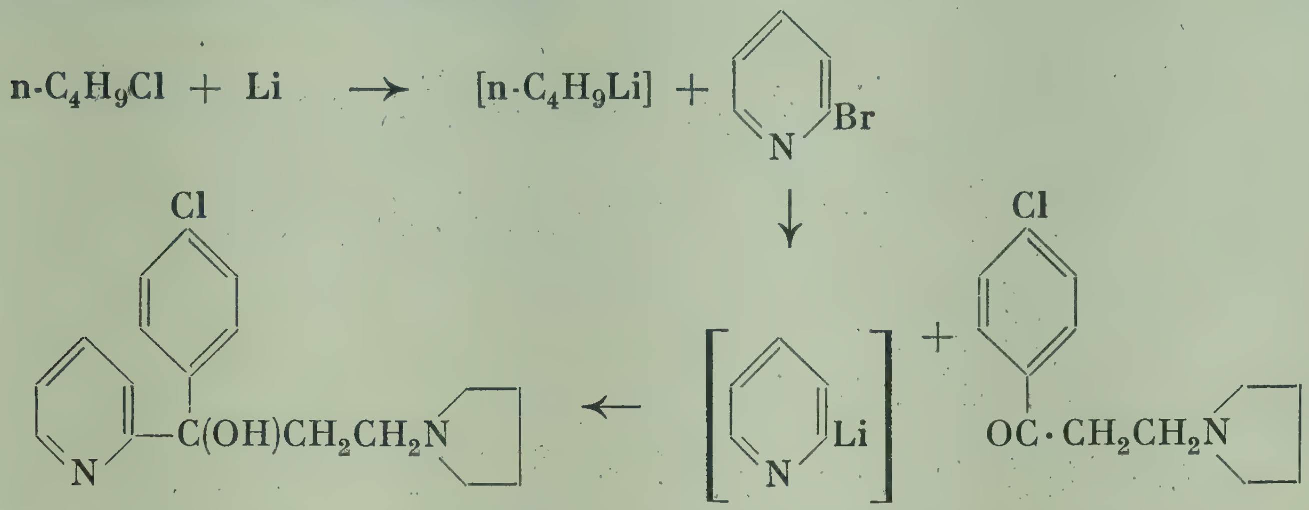
A soln. of p-hydroxyacetophenone in 2 *N* NaOH electrolyzed with Hg-cathode, Pt-anode, —2.2 v, and an initial current of 3.5 amp., at 35°, under N_2, for 20 min. → 2,3-bis-(p-hydroxyphenyl)-2,3-butanediol (startg. m. f. 719). Y: 77%. F. e. s. M. J. Allen, J. Org. Chem. *15,* 435 (1950); Am. Soc. *72,* 114, 117, 3797 (1950).

Lithium *Li*

Tert. alcohols from ketones

CO → C(OH)R

680.



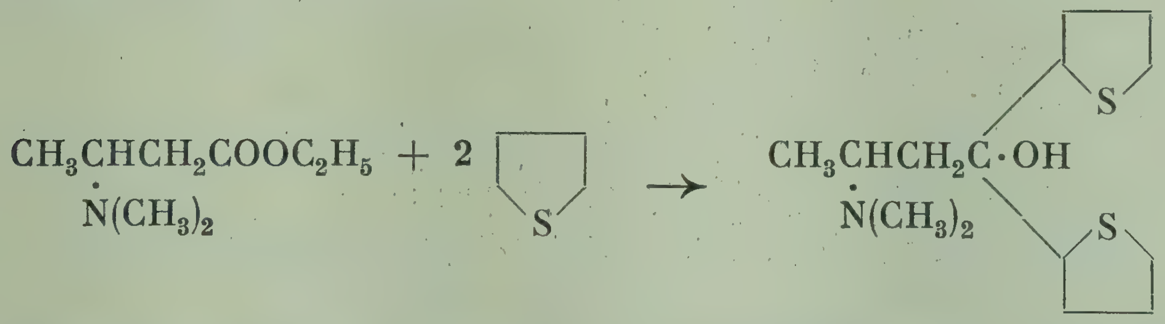
n-Butyl chloride in anhydrous ether added dropwise with stirring under N_2 to freshly sliced Li mixed with a few glass beads, the reaction initiated by warming, and thereafter the rate of addition adjusted to maintain gentle reflux, after the addition (ca. 30 min.) refluxed with stirring for 1 hr., excess Li removed by filtration, the filtrate cooled to —45°, 2-bromopyridine in anhydrous ether added during 15 min., stirring continued for 6 min., p-chlorophenyl-β-pyrrolidinopropiophenone in anhydrous ether added dropwise during 20 min., the temp. allowed to rise to —15°, and stirring continued for 30 min. → 3-pyrrolidino-1-(p-chlorophenyl)-1-(2-pyridyl)propan-1-ol. Y: 69%.—Omitting to remove excess Li reduced the yield of carbinols from p-chlorophenyl ketones, but those from the unsubst. phenyl ketones were not affected. F. e. s. D. W. Adamson and J. W. Billinghurst, Soc. *1950,* 1039.

s. a. J. D. Sculley and N. H. Cromwell, J. Org. Chem. *16,* 94 (1951).

Amino-tert.-alcohols from aminocarboxylic acid esters

COOR → $C(OH)R_2$

681.

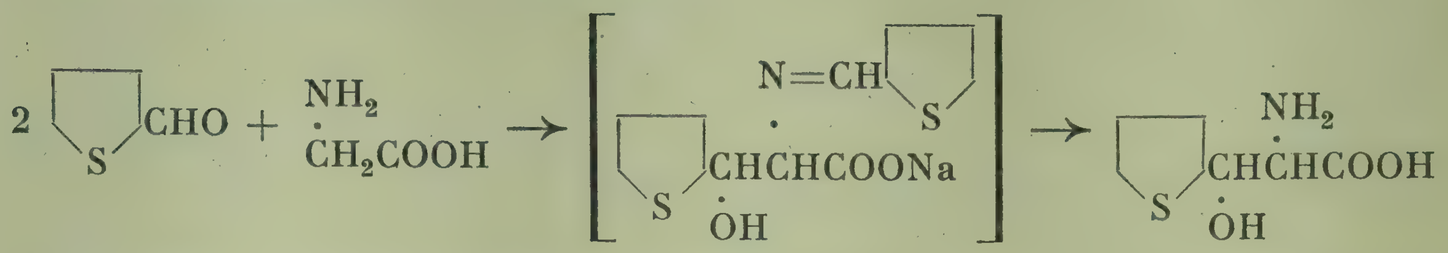


Thiophene in ether added under N_2 to an ethereal soln. of phenyl-Li, prepared from bromobenzene and Li in ether, refluxed 2 hrs., ethyl β-dimethylaminobutyrate in ether added gradually with stirring at —20°, stirring continued for 1 hr. at room temp., and kept overnight → 3-dimethylamino-1,1-di-2′-thienylbutan-1-ol. Y: 71%. F. e. s. D. W. Adamson, Soc. *1950,* 885.

Sodium hydroxide *NaOH*

α-Aminoalcohols from aldehydes ←

682.



2-Thiophenecarboxaldehyde added in one portion at room temp. to a soln. of glycine in aq. NaOH, stirring continued ca. 0.5 hr., allowed to stand 24 hrs., and the Schiff base obtained macerated with concd. HCl in a mortar → 2-thiopheneserine. Y: 79%. G. Weitnauer, G. *81*, 162 (1951); f. e. s. G. *79*, 856 (1949).

Potassium hydroxide *KOH*

Acetylenealcohols from ketones CO → C(OH)C⋮CR

s. *3*, 552; s. a. P. Cadiot and A. Willemart, Bl. *1951*, 100; vinylethynyl derivatives s. I. N. Nazarov et al., Ж. *20*, 2009, 2021 (1950); C. A. *45*, 5636i, 5637f

α-Nitroalcohols from aldehydes CHO → $CH(OH)CH(NO_2)R$

s. *6*, 772

Haloform condensation CO → $C(OH)CCl_3$

s. *4*, 623; s. a. Am. Soc. *72*, 5012 (1950)

Sodium/alcohol *NaOR*

Synthesis of lactones from oxido compounds ←

s. *3*, 554; s. a. E. E. Van Tamelen, G. Van Zyl, and G. D. Zuidema, Am. Soc. *72*, 488 (1950)

Potassium alkoxide *KOR*

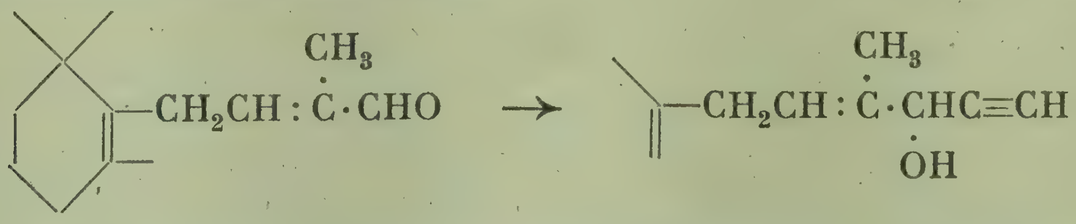
Ethynylalcohols from oxo compounds CO → C(OH)C≡CH

s. *2*, 593; with K-tert-butoxide s. C. Djerassi, R. Yadin, and G. Rosenkranz, Am. Soc. *72*, 5750 (1950)

Lithium/liq. ammonia *Li/NH_3*

Ethynylalcohols from aldehydes CHO → CH(OH)C⋮CH

683.



A rapid stream of dry acetylene passed through a stirred suspension of Li in liq. NH$_3$, cooled in a CO$_2$-alcohol bath; when all the Li had reacted γ-(2,6,6-trimethylcyclohex-1-enyl)-α-methylcrotonaldehyde in ether added dropwise, and stirred overnight, a slow stream of acetylene being passed in throughout → 6-(2′,6′,6′-trimethylcyclohex-1′-enyl)-4-methylhex-4-en-1-yn-3-ol. Y: 75% (33% with Na-acetylide). I. Heilbron et al., Soc. *1949*, 1516; s. a. N. A. Milas et al., Am. Soc. *70*, 1584 (1948); from α,β-ethyleneketones, also with Ca, s. W. Oroshnik and A. D. Mebane, Am. Soc. *71*, 2062 (1949).

Sodium hydrogen carbonate *$NaHCO_3$*

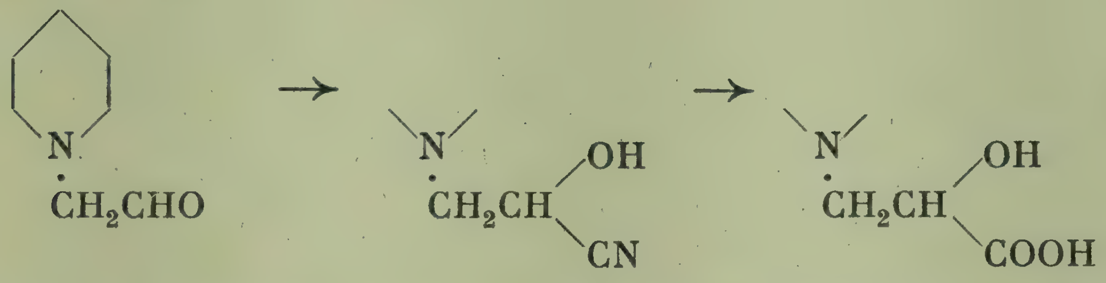
Hydroxymethylation of ketones H → CH_2OH

s. *6,* 749

Sodium cyanide *NaCN*

α-Hydroxycarboxylic acids from aldehydes via cyanohydrins ←

684.



An aq. soln. of piperidinoacetaldehyde hydrochloride added slowly to an ice-cold aq. soln. of NaCN → α-hydroxy-β-piperidinopropionitrile (Y: 95%) refluxed 4 hrs. with concd. HBr, the excess acid removed by distillation at atmospheric pressure until a solid separated, then further concentrated by evaporation on a steam-cone aided by a stream of air → α-hydroxy-β-N-piperidinopropionic acid (Y: 92%). R. Adams and V. V. Jones, Am. Soc. *71*, 3826 (1949).

Sodium hydrogen sulfite *$NaHSO_3$*

Cyanohydrins from oxo compounds CO → C(OH)CN

from aldehydes s. *4,* 625; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. *73,* 1414 (1951); from ketones s. M. Stoll, L. Ruzicka, and C. F. Seidel, Helv. *33,* 1245 (1950)

Diethylamine *$(C_2H_5)_2NH$*

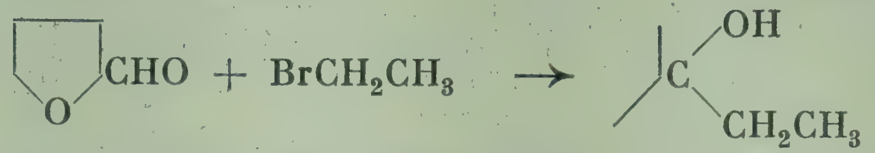
α-Nitroalcohols from aldehydes CHO → $CH(OH)CH(NO_2)R$

s. *3,* 559; s. a. D. J. Cook, D. Dock, and R. Shrontz, Am. Soc. *72,* 4989 (1950)

Magnesium ***Mg***

Sec. alcohols from aldehydes
CHO → CH(OH)R

685.

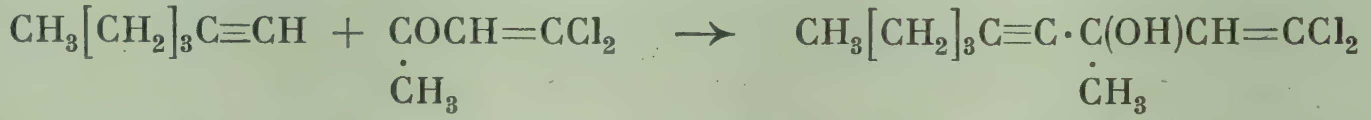


Furfural in ether added with stirring at ca. —15° to ethereal ethyl-MgBr, heated 0.5 hr. on a steam bath, cooled, decomposed with water, the ether extract washed with 40%-$NaHSO_3$, and distilled in the presence of 10-12 drops of aniline to eliminate traces of acid → ethyl-2-furylcarbinol. Y: 89%. F. e. with lower yields s. Y. K. Yur'ev and I. P. Gragerov, Ж. *19,* 724 (1949); C. A. *44,* 1092c.

α,β-Ethylenealcohols
s. *6,* 764

Acetylenealcohols from oxo compounds
CO → C(OH)C⋮CR

686.



$$CH_3[CH_2]_3C{\equiv}CH + \underset{CH_3}{C}OCH{=}CCl_2 \rightarrow CH_3[CH_2]_3C{\equiv}C\cdot \underset{CH_3}{C}(OH)CH{=}CCl_2$$

An ethereal soln. of 1-hexyne added with ice-cooling during 2 hrs. to ethereal ethyl-MgBr, refluxed 3 hrs., then methyl 2,2-dichlorovinyl ketone (prepn. s. 814) in dry ether added slowly with cooling, and allowed to stand overnight → 1,1-dichloro-3-methylnon-1-en-4-yn-3-ol. Y: 85%.—The condensation with Na-acetylide in liq. NH_3 was not successful in this case. F. e. s. I. M. Heilbron, E. R. H. Jones, and M. Julia, Soc. *1949,* 1430; s. a. P. Karrer and P. Schneider, M. *81,* 111 (1950).

Amino-tert.-alcohols from aminoketones
CO → C(OH)R

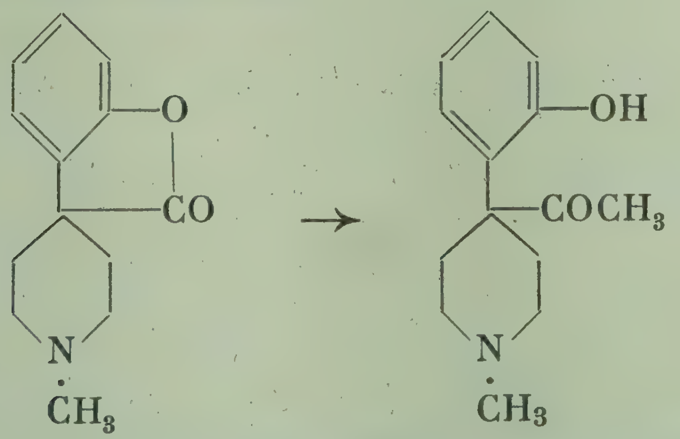
s. *1,* 679; s. a. A. W. Ruddy and J. S. Buckley, Jr., Am. Soc. *72,* 718 (1950); J. J. Denton et al., Am. Soc. *72,* 3795 (1950)

Diols from lactones
C

s. *5,* 477; s. a. W. Baker, R. F. Curtis, and J. F. W. McOmie, Soc. *1951,* 76

Hydroxyketones from lactones

687.



1-Methyl-4-o-hydroxyphenylpiperidine-4-carboxylic acid lactone hydrobromide (prepn. s. 240) added to ice-cold ethereal methyl-

MgBr, stirred 1/2 hr. in the cold, then 10 min. under reflux → 1-methyl-4-o-hydroxyphenyl-4-piperidyl methyl ketone. Y: 82%. F. e. s. H. Kägi and K. Miescher, Helv. *32,* 2489 (1949).

Magnesium/magnesium iodide *Mg/MgI_2*

Pinacols ←

s. *1,* 689; s. a. R. Moubasher, Soc. *1950,* 2243

Calcium/liq. ammonia *Ca/NH_3*

Ethynylalcohols from aldehydes CHO → CH(OH)C⋮CH

s. *6,* 683

Zinc *Zn*

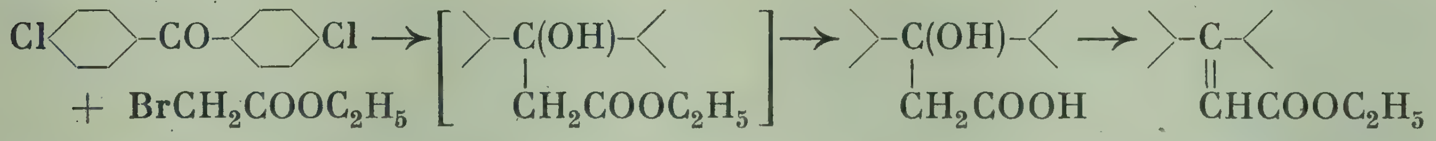
Reformatskii synthesis of acetylenealcohols from oxo compounds CO → C(OH)C⋮CH

688. $CH_3CH{=}CHCHO + BrCH_2C{\equiv}CH \rightarrow CH_3CH{=}CHCH(OH)CH_2C{\equiv}CH$

A mixture of freshly distilled crotonaldehyde and propargyl bromide in dry ether added to Zn wool covered with benzene, a part of which has been distilled off to remove traces of water, and refluxed 5 min. → 5-hepten-1-yn-4-ol. Y: 67%.—Occasionally, when the reaction is difficult to start, addition of a little $HgCl_2$ proves effective. F. e. s. H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, Soc. *1949,* 2696; *1950,* 3634; s. a. R. Golse, J. Gavarret, and G. Demange, Bl. *1950,* 285; P. Karrer and C. H. Eugster, Helv. *34,* 28 (1951).

Reformatskii synthesis of carboxylic acid esters Dehydration with simultaneous esterification ←

689.



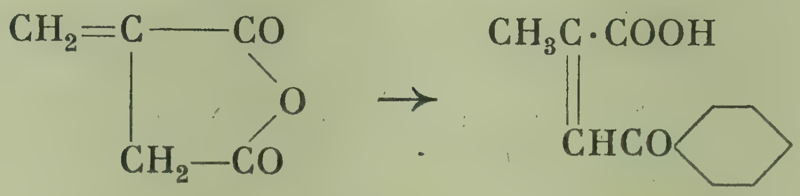
Excess 30-mesh Zn, activated according to Fieser and Johnson, Am. Soc. *62,* 575 (1940), and a crystal of iodine added to a soln. of 4,4′-dichlorobenzophenone and excess ethyl bromoacetate in anhydrous benzene-toluene, refluxed with stirring for ca. 30 min. until the exothermic reaction starts, cooled with cold water during the next 20 min., refluxed 2 more hrs. after the reaction has subsided, and the ester, so obtained, hydrolyzed by refluxing with KOH in ethanol-water for 2 hrs. → *β,β*-bis-(p-chlorophenyl)hydracrylic acid (Y: 92.3%) dissolved in abs. alcohol, anhydrous HCl passed through for 4 hrs., and refluxed during the last hr. → ethyl *β,β*-bis-(p-chlorophenyl)acrylate (Y: 83.5%). J. F. Freeman and E. D. Amstutz, Am. Soc. *72,* 1522 (1950); Reformatskii synthesis s. a. R. C. Gilmore, Jr., and W. J. Horton, Am. Soc. *73,* 1411 (1951).

Aluminum chloride *$AlCl_2$*

Ketocarboxylic acids from dicarboxylic acid anhydrides ←

s. *1*, 519; *2*, 601; *3*, 566; *4*, 635 a; s. a. J. A. McRae, R. A. B. Bannard, and R. B. Ross, Can. J. Research *28B*, 73 (1950); in s-tetrachloroethane s. R. R. Burtner and J. M. Brown, Am. Soc. *73*, 897 (1951)

690.



with migration of a carbon double bond. A soln. of itaconic anhydride in dry benzene treated with finely powdered anhydrous $AlCl_3$, the reaction started by slight warming, and after subsiding refluxing continued for 3 hrs. → β-benzoyl-α-methylacrylic acid. Y: 78%. S. Dixon, H. Gregory, and L. F. Wiggins, Soc. *1949*, 2139.

Addition to Nitrogen and Carbon CC ⇓ NC

Without additional reagents *w.a.r.*

1-Acyl-1,2-dihydroquinaldonitriles (Reissert compounds) from carboxylic acid chlorides ←

s. *6*, 122

Pyridine *C_5H_5N*

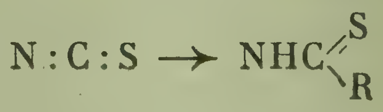
Cyanoformamides from isocyanates N:C:O → NHCOCN

691. $2\ HCN + OCN[CH_2]_6NCO \rightarrow NC{\cdot}CONH[CH_2]_6NHCO{\cdot}CN$

Anhydrous HCN added to a soln. of 252 gm. hexamethylene diisocyanate in toluene, cooled, pyridine added, and allowed to stand overnight → 290 gm. N,N′-dicyanoformylhexamethylenediamine. F. e. s. S. Petersen, A. *562*, 205 (1949).

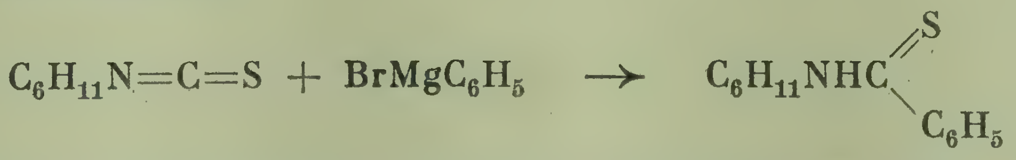
Magnesium *Mg*

Subst. carboxylic acid thioamides from isothiocyanates



$N{:}C{:}S \rightarrow NHC\begin{smallmatrix}{\diagup}S\\ {\diagdown}R\end{smallmatrix}$

692.



$C_6H_{11}N{=}C{=}S + BrMgC_6H_5 \rightarrow C_6H_{11}NHC\begin{smallmatrix}{\diagup}S\\ {\diagdown}C_6H_5\end{smallmatrix}$

Cyclohexyl isothiocyanate in ether added below 5° with stirring to ethereal phenyl-MgBr, stirring continued at 5° for 1 hr., then allowed to come to room temp. → N-cyclohexylthiobenzamide. Y: 88%. F. e. s. G. Alliger et al., J. Org. Chem. *14*, 962 (1949).

Zinc chloride *$ZnCl_2$*

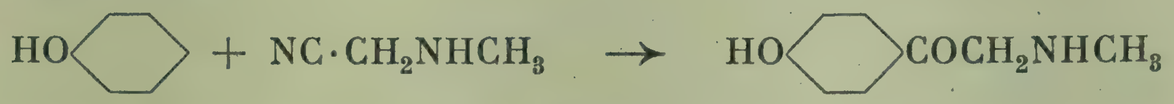
Hoesch synthesis of ketones CN → COR

s. *1*, 618; *2*, 606/7; s. a. W. B. Whalley, Soc. *1951*, 665

Aluminum chloride *$AlCl_3$*

Aminoketones from aminonitriles
Hoesch synthesis CN → COR

693.



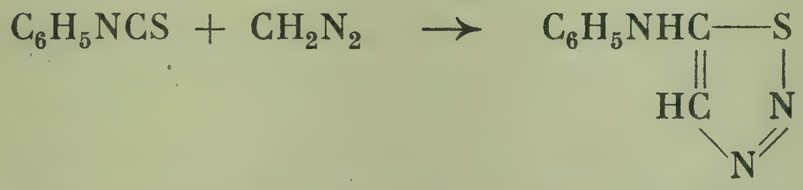
Aminoketones from aminonitriles. Phenol and methylaminoacetonitrile hydrochloride added all at once with shaking to a soln. of $AlCl_3$ in nitrobenzene, then a current of dry HCl passed through at 20-30° with stirring for 3 hrs. → p-hydroxy-ω-(methylamino)acetophenone. Y: 75%. F. e. s. M. Asscher, R. *68*, 960 (1949).

Addition to Sulfur and Carbon CC ⇓ SC

Without additional reagents *w.a.r.*

1,2,3-Thiadiazoles from isothiocyanates and diazomethane ○

694.



Cold ethereal diazomethane added to ethereal phenylisothiocyanate, then allowed to stand at room temp. for 1 hr. and at 0-5° overnight → 5-anilino-1,2,3-thiadiazole. Y: 60%. J. C. Sheehan and P. T. Izzo, Am. Soc. *71*, 4059 (1949).

Addition to Carbon CC ⇓ CC

Without additional reagents *w.a.r.*

Subst. succinic acid anhydrides from maleic acid anhydride ←

s. *5*, 487; s. a. R. T. Arnold, R. W. Amidon, and R. M. Dodson, Am. Soc. *72*, 2871 (1950); C. S. Rondestvedt, Jr., Org. Synth. *31*, 85 (1951)

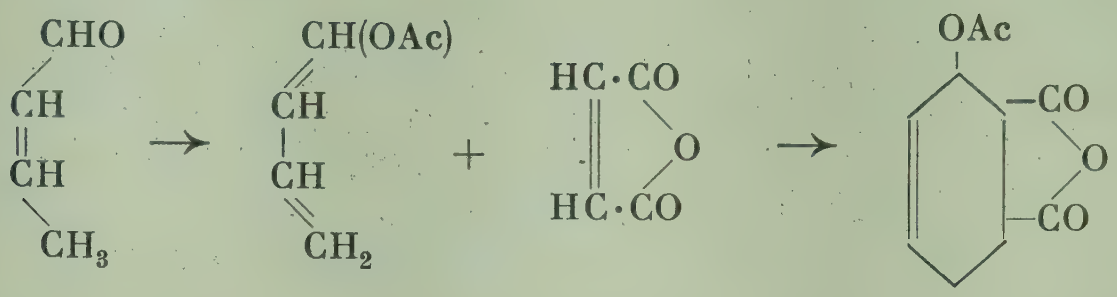
Diene synthesis
Diels-Alder reaction ○

s. *1*, 526-9; *2*, 609-11; *3*, 576; s. a. G. O. Schenck, B. *82*, 123 (1949); with unsym. addends s. K. Alder et al., A. *564*, 79, 120 (1949); with naphthalenes s. M. C. Kloetzel, R. P. Dayton, and H. L. Herzog, Am. Soc.

72, 273, 1991 (1950); with α,β,γ,δ-unsatd. carboxylic acids s. N. C. Deno, Am. Soc. *72*, 4057 (1950)

Diene synthesis via enolesters Polymerization inhibitors

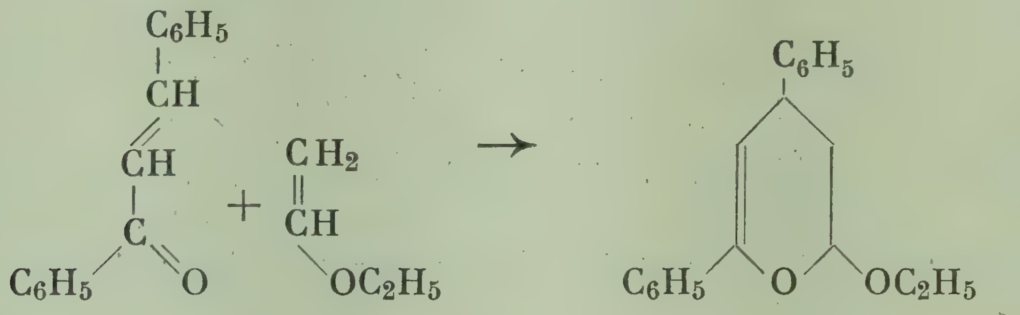
695.



Crotonaldehyde, acetic anhydride, and anhydrous Na-acetate heated 5 hrs. under reflux at 160°, cooled, filtered, distilled, a little thionine as polymerization inhibitor and maleic anhydride in acetone added, and heated 0.5 hr. on a water bath → 3-acetoxy-1,2,3,6-tetrahydrophthalic anhydride (startg. m. f. 864). Y: up to 95% based on reacted maleic anhydride. F. e. and inhibitors s. W. Flaig, A. *568*, 1 (1950).

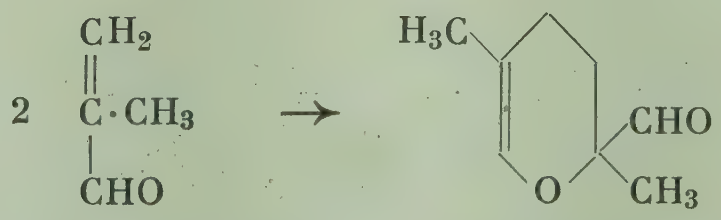
Pyrans, dihydro- from α,β-ethyleneoxo compounds

696.



Benzalacetophenone, ethyl vinyl ether, and a small amount of hydroquinone (as polymerization inhibitor) heated 13 hrs. at 180° in an autoclave → 2-ethoxy-4,6-diphenyl-3,4-dihydro-1,2-pyran (startg. m. f. 172). Y: 74%. F. e. s. R. I. Longley, Jr., and W. S. Emerson, Am. Soc. *72*, 3079 (1950).

697.

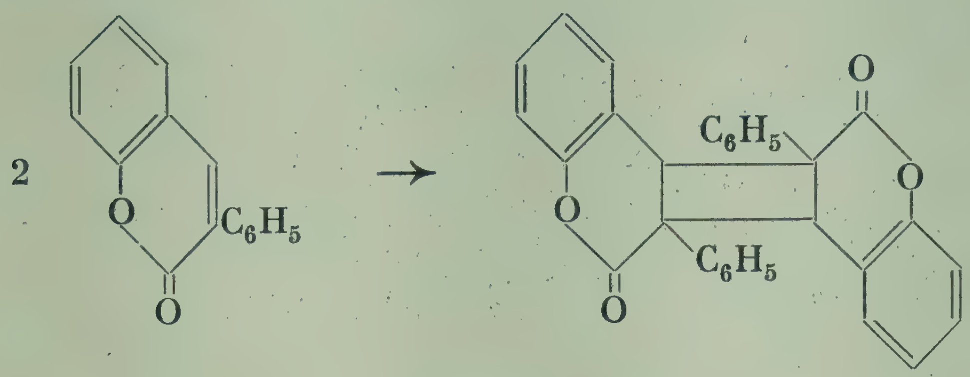


Dimers by polymerization reaction. Freshly distilled methacrylaldehyde containing a little hydroquinone heated in a sealed tube at 140-150° for 44 hrs. → 3,4-dihydro-2,5-dimethyl-2H-pyran-2-carboxaldehyde. Y: 89%. G. G. Stoner and J. S. McNulty, Am. Soc. *72*, 1531 (1950).

Light

Cyclobutane ring from ethylene derivatives Photodimerization

698.



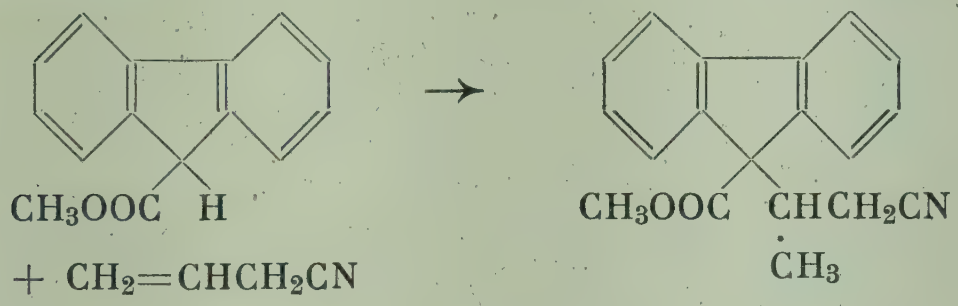
3-Phenylcoumarin in benzene exposed to sunlight for 1 month → photodimer. Y: ca. 90%. F. e. s. A. Schönberg et al., Soc. *1950*, 374.

Potassium hydroxide *KOH*

C-Cyanoethylation

$\mathrm{H} \rightarrow \mathrm{CH_2CH_2CN}$

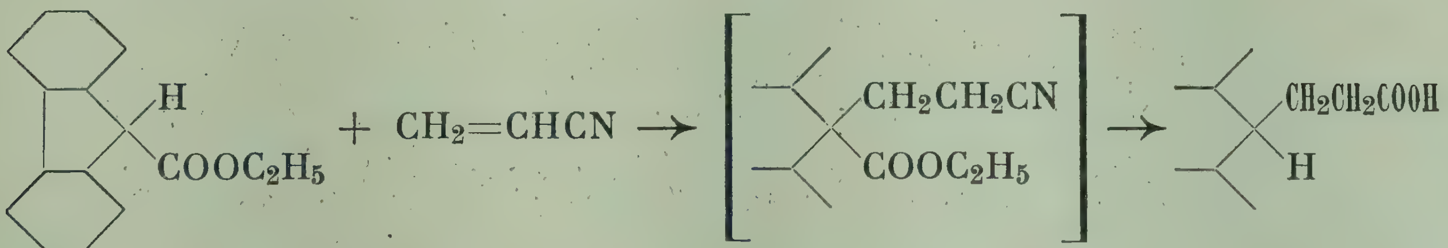
699.



Dioxane, KOH, allyl cyanide, and methyl fluorene-9-carboxylate mixed in that order, and allowed to stand at room temp. for 4 days → 2-(9′-carbomethoxy-9′-fluorenyl)propyl cyanide. Y: 73%.—2-Methoxyethanol can be used in place of dioxane as a solvent. Other reaction conditions (s. original paper) were not successful. S. H. Tucker, Soc. *1949*, 2182.

Subst. propionic acids from carboxylic acid esters via α-(2-cyanoethyl)carboxylic acid esters

700.

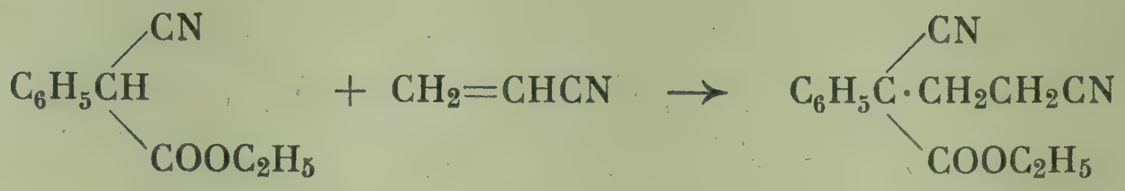


Ethyl 9-fluorenecarboxylate, then vinyl cyanide added to a soln. of KOH in 2-methoxyethanol, after 15 min. treated with aq. 10 *N* KOH, then with more 2-methoxyethanol, and boiled 30 min. → β-9-fluorenepropionic acid. Y: 90%. Also isolation of the intermediates s. A. Campbell and S. H. Tucker, Soc. *1949*, 2623; with Triton B s. T. Holbro and E. Tagmann, Helv. *33*, 2178 (1950).

Potassium hydroxide/alcohol

C-Cyanoethylation of α-cyanocarboxylic acid esters

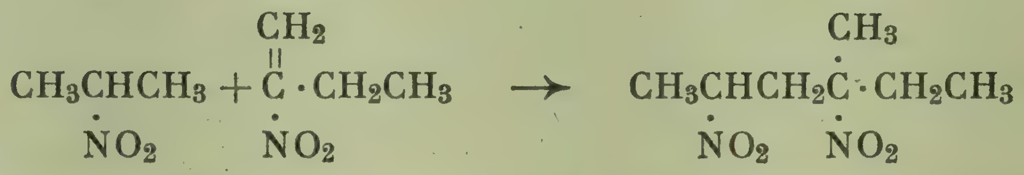
701.



A soln. of acrylonitrile in *tert*-butanol added dropwise to a soln. of ethyl phenylcyanoacetate in *tert*-butanol at 40-45°, while some methanolic 30%-KOH is added in 2 portions; when the exothermic reaction subsides, warmed in a water bath at 40-45° for 1 hr., then allowed to stand overnight → α-phenyl-α-carbethoxyglutaronitrile. Y: 69-83%. E. C. Horning and A. F. Finelli, Am. Soc. *71*, 3204 (1949); Org. Synth. *30*, 80 (1950).

β-Dinitro compounds, aliphatic

702.



$$CH_3\underset{NO_2}{C}HCH_3 + \overset{CH_2}{\underset{NO_2}{C}}\cdot CH_2CH_3 \longrightarrow CH_3\underset{NO_2}{C}HCH_2\overset{CH_3}{\underset{NO_2}{C}}\cdot CH_2CH_3$$

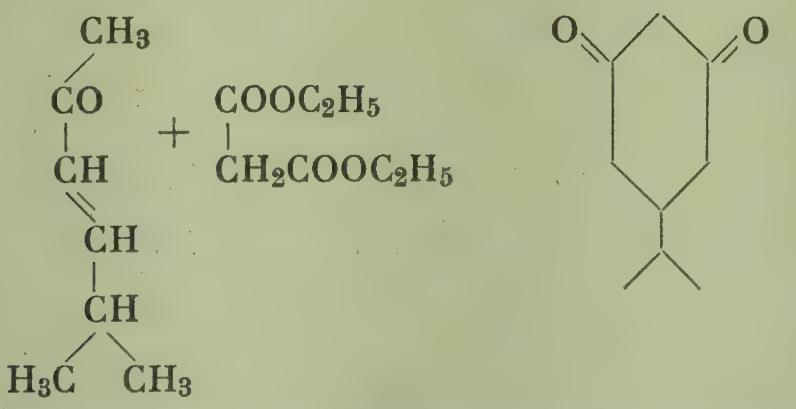
Fresh 2-nitro-1-butene added at 18-20° in small portions with vigorous stirring over a period of 30 min. to the K-salt of 2-nitropropane, prepared with alc. KOH, dil. with water, and acidified with acetic acid → 3,5-dinitro-3-methylhexane. Crude Y: 90%. F. e. s. C. T. Bahner and H. T. Kite, Am. Soc. *71*, 3597 (1949).

Sodium/alcohol *NaOR*

Michael addition ←

s. *5*, 494; s. a. D. Ginsburg and R. Pappo, Soc. *1951*, 938; D. L. Turner, Am. Soc. *73*, 1284 (1951)

703.

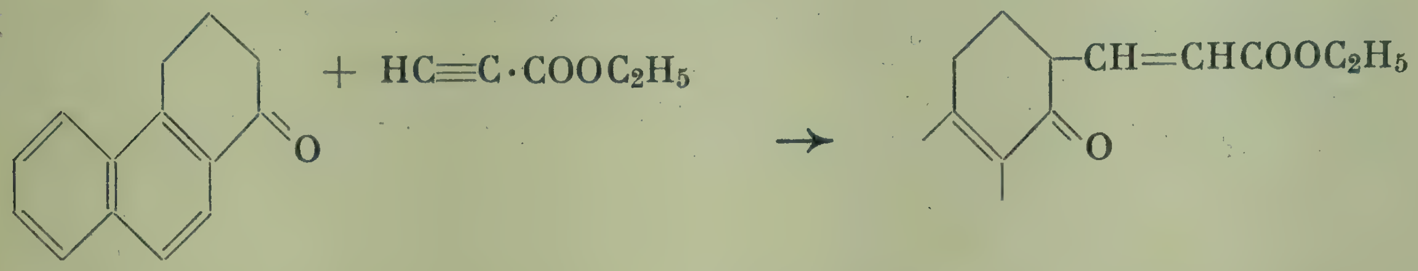


Cyclohexanediones. Ethyl malonate and isobutylideneacetone added to a soln. of Na in abs. ethanol, refluxed 1 hr., additional abs. ethanol added, refluxing continued for 2 more hrs., aq. KOH added, and refluxed an additional 6 hrs. → 5-isopropyl-1,3-cyclohexanedione. Y: 80%. R. L. Frank and H. K. Hall, Jr., Am. Soc. *72*, 1645 (1950).

Sodium amide *$NaNH_2$*

α,β-Ethylene-δ-ketocarboxylic acid esters from ketones and propiolic esters ←

704.



Semiaromatic ketones, in the presence of NaNH$_2$, undergo a Michael reaction with propiolic esters, whereas these esters are added to the carbonyl group of purely alicyclic ketones to form α,β-acetylenic γ-hydroxyesters.—E: 1-Keto-1,2,3,4-tetrahydrophenanthrene allowed to react with ethyl propialote and NaNH$_2$ in liq. NH$_3$ → ethyl β-(1-keto-1,2,3,4-tetrahydro-2-phenanthrene)acrylate. Y: 83%. F. e. s. W. E. Bachmann, E. K. Raunio, and G. I. Fujimoto, Am. Soc. *72*, 2533, 2530 (1950).

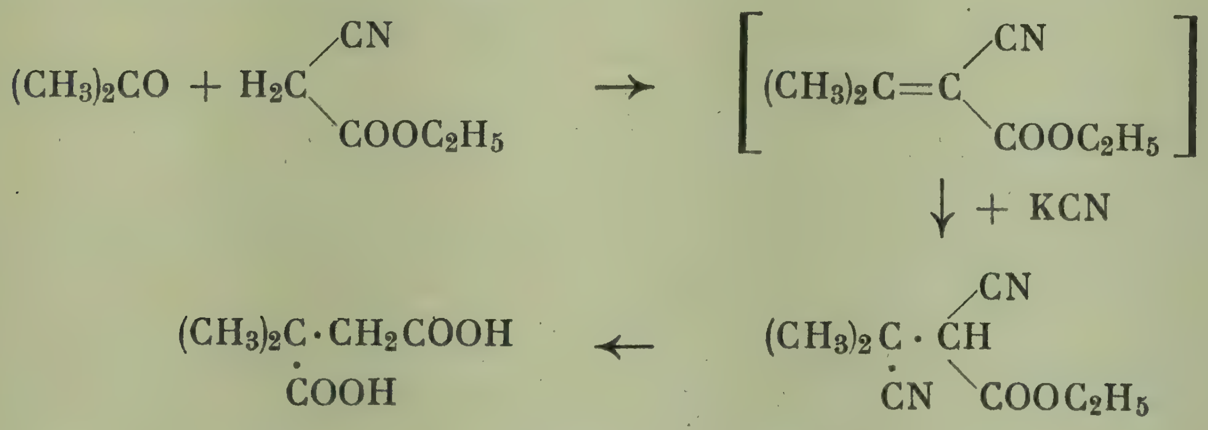
Potassium cyanide *KCN*

Nitriles from ethylene derivatives C:C → CHC(CN)

s. *3*, 583; s. a. P. Kurtz, A. *572*, 23 (1951); A. C. Cope and S. W. Fenton, Am. Soc. *73*, 1668 (1951)

Unsym. subst. succinic acids Dicarboxylic acids from dicyanodicarboxylic acid esters

705.



A mixture of dry acetone, ethyl cyanoacetate, pyridine, and glacial acetic acid refluxed 1 hr., abs. ethanol added; as soon as active boiling subsides, KCN added, and refluxed ca. 1 hr. more → ethyl α,β-dicyano-β-methylbutyrate (Y: 70%) refluxed with concd. HCl for 8 hrs. → α,α-dimethylsuccinic acid (Y: 76%). F. e. s. P. A. S. Smith and J. P. Horwitz. Am. Soc. *71*, 3418 (1949); s. a. E. J. Cragoe, Jr., C. M. Robb, and J. M. Sprague, J. Org. Chem. *15*, 381 (1950).

Triton B ←

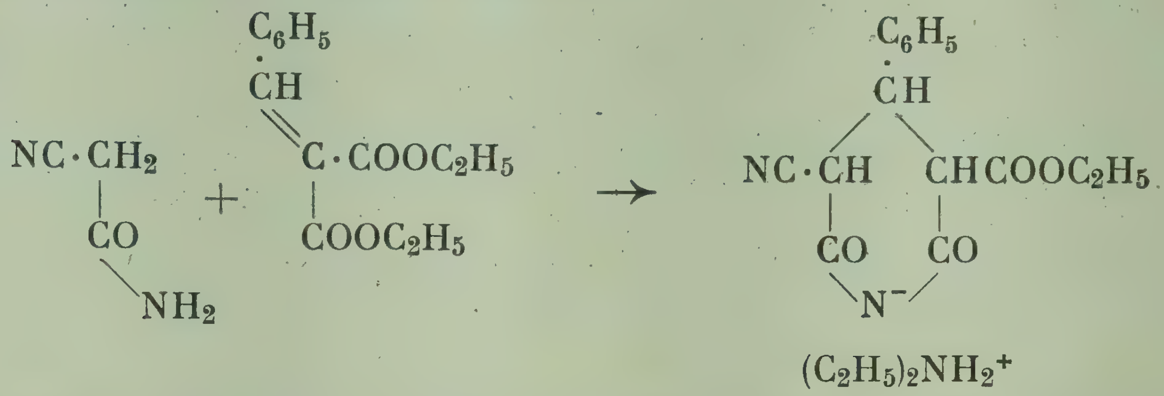
C-Cyanoethylation H → CH_2CH_2CN

s. *5*, 497; s. a. N. A. Acara and R. Levine, Am. Soc. *72*, 2864 (1950); W. E. Bachmann and L. B. Wick, Am. Soc. *72*, 3388 (1950)

Diethylamine *$(C_2H_5)_2NH$*

Pyridine ring from cyanoacetamides ○

706.

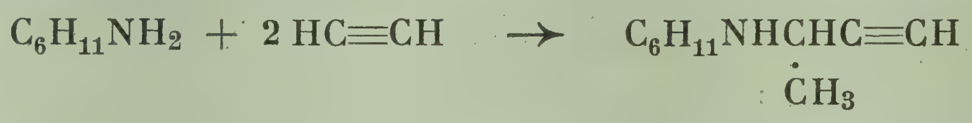


A suspension of 0.8 gm. cyanoacetamide in 2.5 gm. ethyl benzylidenemalonate treated with diethylamine, after 3 days dissolved in alcohol by heating, some fresh diethylamine added, and worked up on the following day → 2.8 gm. diethylammonium salt of 3-carbethoxy-5-cyano-2,6-diketo-4-phenylpiperidine. F. e. s. N. Palit, J. Indian Chem. Soc. *26*, 501 (1949).

Cuprous chloride *CuCl*

Synthesis of 3-amino-1-butynes ←

707.



$$C_6H_{11}NH_2 + 2\,HC{\equiv}CH \rightarrow C_6H_{11}NH\underset{\displaystyle CH_3}{CH}C{\equiv}CH$$

Cyclohexylamine and CuCl in tetrahydrofuran treated at 106° with acetylene-N_2 under pressure → 3-cyclohexylamino-1-butyne. Y: 70%. F. e. s. J. D. Rose et al., Soc. *1949*, 780, 792.

Cuprous iodide/magnesium *CuI/Mg*

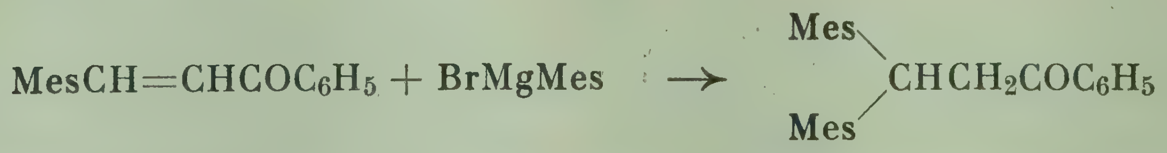
tert-Alkyl-α-cyanoacetic esters from alkylidene-α-cyanoacetic esters ←

s. *2*, 616; cf. E. R. Alexander, J. D. McCollum, and D. E. Paul, Am. Soc. *72*, 4791 (1950)

Magnesium *Mg*

Synthesis of hydrocarbons from ethylene derivatives C:C → CHCR

708.



$$MesCH{=}CHCOC_6H_5 + BrMgMes \rightarrow \begin{matrix} Mes \\ & CHCH_2COC_6H_5 \\ Mes \end{matrix}$$

The presence of a mesityl radical in the β-position of an α,β-ethylene ester or unhindered ketone does not prevent conjugate addition of mesityl-Mg-bromide.—E: A soln. of mesitalacetophenone (prep. s. 740) in dry benzene-ether added to a Grignard reagent, prepared from bromomesitylene, Mg, and dry ether, then stirred and refluxed 2 hrs., and hydrolyzed by a satd. soln. of NH_4Cl → β,β-dimesitylpropiophenone. Y: 84%. R. C. Fuson and H. L. Jackson, Am. Soc. *72*, 1637 (1950).

Alumina/silica *Al_2O_3/SiO_2*

Alkylation of the nucleus with ethylene derivatives

s. *3*, 585; s. a. V. N. Ipatieff, E. E. Meisinger, and H. Pines, Am. Soc. *72*, 2772 (1950)

Aluminum chloride *$AlCl_3$*

Polyhalides C:C → CHalCR

Prins reaction

s. *3*, 586; *4*, 660; s. a. H. J. Prins, R. *69*, 1003 (1950)

Acyl peroxides *$(RCOO)_2$*

Addition of polyhalides to unsaturated carbon carbon bonds ←

addition to double bonds s. *3*, 587; *4*, 665; G. Dupont, R. Dulou, and P. Guantin, Bl. *1951*, 59; addition to triple bonds s. M. S. Kharasch, J. J. Jerome, and W. H. Urry, J. Org. Chem. *15*, 966 (1950)

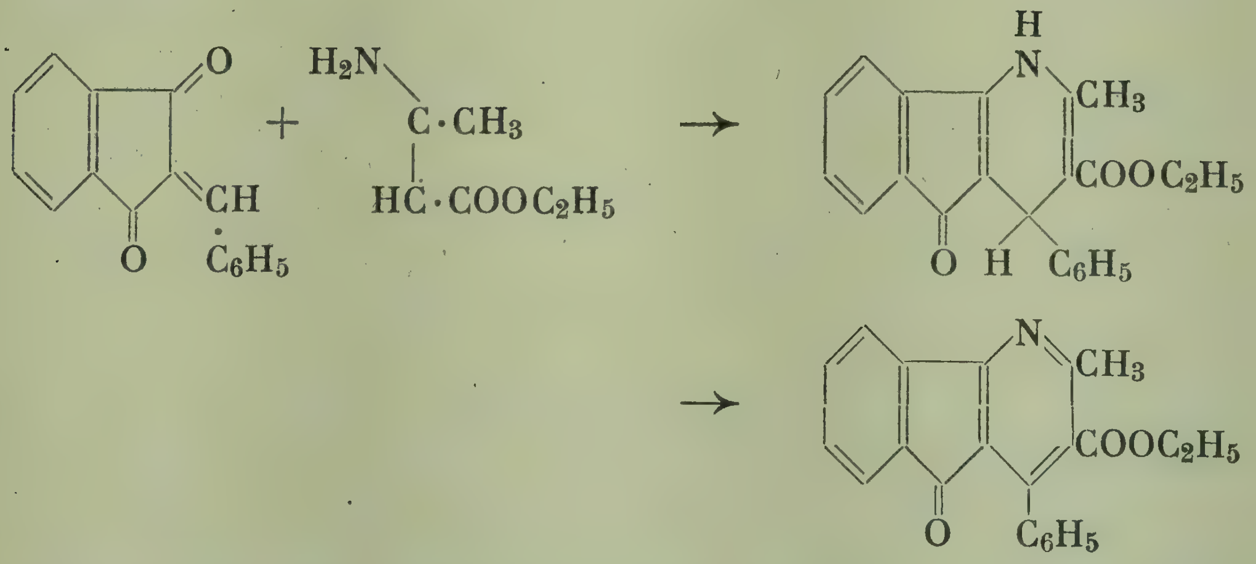
Acetic acid *CH_3COOH*

Pyridine ring synthesis ○

4-Azafluorenones

Dehydrogenation

709.



A soln. of benzylideneindane-1,3-dione in acetic acid treated at the boiling point with ethyl β-aminocrotonate → ethyl 1-phenyl-3-methyl-1,4-dihydro-4-azafluorenone-2-carboxylate (Y: 87%) dissolved in warm acetic acid and treated with aq. CrO_3 for 5 min. → ethyl 1-phenyl-3-methyl-4-azafluorenone-2-carboxylate (Y: 88%). F. e. s. V. Petrow et al., Soc. *1949*, 2134, 2128.

Sulfuric acid H_2SO_4

Synthesis of hydrocarbons from ethylene derivatives

C:C → CHCR

Isocyclics

s. *5,* 506; s. a. R. Truffault and Y. Monteils, Bl. *1951,* 97

Alkylation of thiophenes with olefins

s. *5,* 507; cf. H. Pines, B. Kvetinskas, and J. A. Vesely, Am. Soc. *72,* 1568 (1950)

m-Dioxanes from ethylene derivatives

○

s. *4,* 637

Hydrofluoric acid *HF*

One-step indanone ring synthesis

s. *6,* 819

Cobalt carbonyl $Co(CO)_4$

Aldehydes from ethylene derivatives
Synthesis with addition of 1 C-atom

C:C → CHC(CHO)

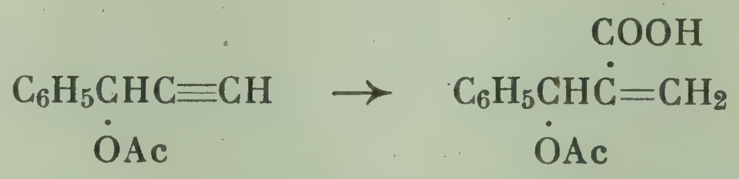
s. *4,* 667; s. a. W. E. Parham and H. E. Holmquist, Am. Soc. *73,* 913 (1951)

Nickel carbonyl $Ni(CO)_4$

α,β-Ethylenecarboxylic acids from acetylene derivatives

C⋮C → CH:C·COOH

710.



$$C_6H_5\underset{OAc}{CH}C\equiv CH \rightarrow C_6H_5\underset{OAc}{CH}\overset{COOH}{C}=CH_2$$

The reaction between monosubst. acetylene derivatives, Ni-carbonyl, and water in the presence of acids leads to the formation of α-subst. acrylic acids. The products from β,γ-acetylenic carbinols cyclize spontaneously to lactones. With α,β-acetylenic carbinols, it is preferable to employ the acetates rather than the free alcohols.—E:Phenylethynylcarbinyl acetate, ethanol, glacial acetic acid, and water allowed to react at 70° with $Ni(CO)_4$ in ethanol → 3-acetoxy-3-phenylprop-1-ene-2-carboxylic acid. Y: 50%. F. e. s. E. R. H. Jones, T. Y. Shen, and M. C. Whiting, Soc. *1950,* 230; Soc. *1951,* 48; cf. E. D. Bergmann and E. Zimkin, Soc. *1950,* 3455.

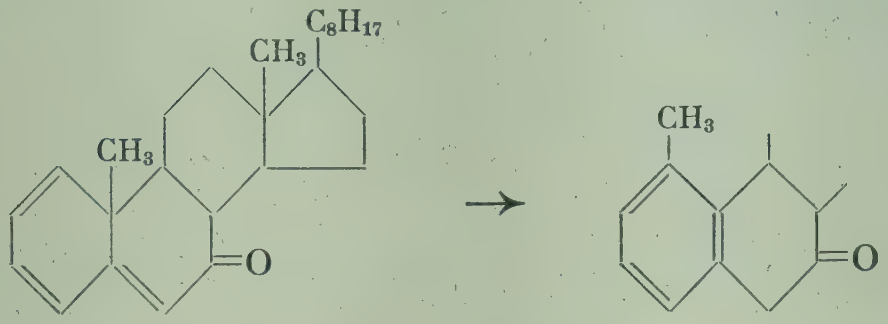
Rearrangement

Hydrogen/Carbon Type **CC↶HC**

Without additional reagents *w.a.r.*

Aromatization ←

711.

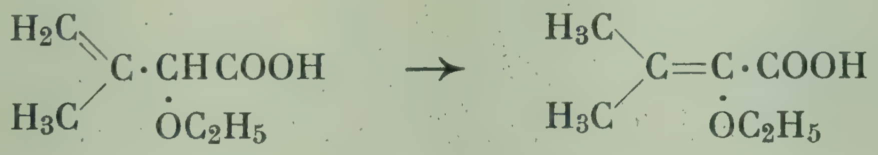

C8H17
CH3
CH3
=O
→
CH3
=O

200 mg. $\Delta^{1,3,5(6)}$-cholestatrien-7-one slowly heated to 160°, and kept at this temp. for 15 min. → 130 mg. 1-methyl-$\Delta^{1,3,5(10)}$-nor^{10}-cholestatrien-7-one. P. Karrer and A. R. Naik, Helv. *32*, 2392 (1949).

Sodium hydroxide *NaOH*

Migration of carbon double bonds
Prototropic change ←

712.


H2C
C·CHCOOH
H3C
OC2H5
→
H3C
C=C·COOH
H3C
OC2H5

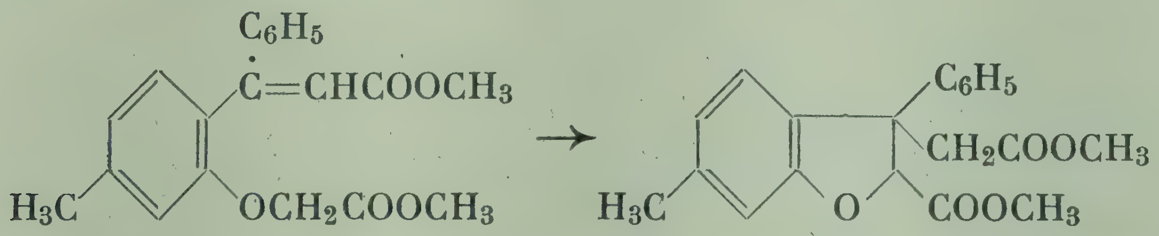
0.82 gm. α-ethoxy-β-methylenebutyric acid heated 24 hrs. with aq. 5 *N* NaOH at 100° → 0.7 gm. α-ethoxy-β,β-dimethylacrylic acid. F. e. s. L. N. Owen and M. U. S. Sultanbawa, Soc. *1949*, 3089.

Sodium/alcohol *NaOR*

Nitrocyclopropane ring opening ↺
s. *6*, 225

Heterocyclics by internal Michael addition ○

713.


C6H5
C=CHCOOCH3
H3C
OCH2COOCH3
→
C6H5
CH2COOCH3
H3C
O
COOCH3

A mixture of methyl 4-methyl-β-phenylcoumarinate 0-acetic acid methyl ester with 4 drops of a concd. soln. of Na-methoxide in methanol warmed to 60°, after which the temp. rises spontaneously to ca. 90° during 4 min. → methyl 3-carbomethoxymethyl-6-methyl-3-phenyl-2,3-dihydrocoumarilate. Y: 80%. F. e. s. C. F. Koelsch and C. R. Stephens, Jr., Am. Soc. *72*, 2209 (1950).

Sodium amide *$NaNH_2$*

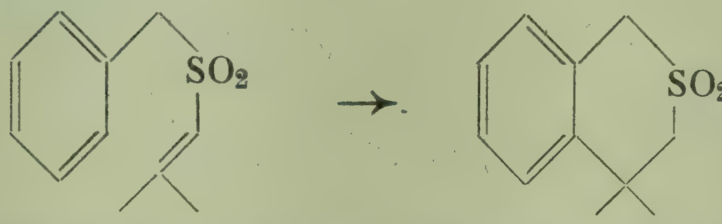
4-Amino-2-hydroxypyridine ring from β-acyliminonitriles

s. *5*, 511; s. a. G. A. Reynolds et al., J. Org. Chem. *16*, 165 (1951)

Boron fluoride/sulfuric acid *BF_3/H_2SO_4*

Cycloisomerization

714.



A soln. of benzyl 2-methylpropenyl sulfone in 95%-H_2SO_4 containing ca. 12% BF_3 heated 3 hrs. at 70° → 5,5-dimethyl-3,4-benzothiacyclohexane 1,1-dioxide. Y: 75%. F. e. s. H. J. Backer and N. Dost, R. *68*, 1143 (1949).

Aluminum chloride *$AlCl_3$*

Migration ←

of carbon double bonds

s. *6*, 690

Aluminum chloride/hydrochloric acid *$AlCl_3/HCl$*

of alkyl groups

s. *6*, 833

Hydrazine/sodium/alcohol *$H_2N{\cdot}NH_2/NaOR$*

of carbon double bonds

s. *6*, 117

Phosphoric acid *H_3PO_4*

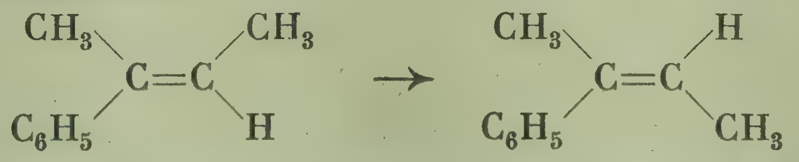
Ring closure to isocyclics ○

s. *5*, 515; without H in the vinyl radical of the starting material s. Ж. *20*, 1441 (1950); C. A. *45*, 1964f

p-Toluenesulfonic acid *TsOH*

cis-trans Rearrangement ←

715.



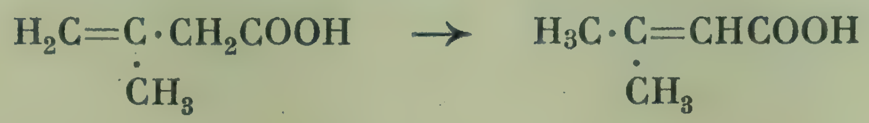
$$(CH_3)(C_6H_5)C{=}C(CH_3)(H) \rightarrow (CH_3)(C_6H_5)C{=}C(H)(CH_3)$$

13.5 gm. *cis*-2-phenyl-2-butene slowly fractionated at 29.5 mm in the presence of a small amount of p-toluenesulfonic acid → 11.4 gm. *trans*-2-phenyl-2-butene.—The lower boiling *trans*-isomer can be distilled from the continually equilibrating mixture. D. J. Cram, Am. Soc. *71*, 3883 (1949).

Sulfuric acid *H_2SO_4*

Migration of carbon double bonds ←

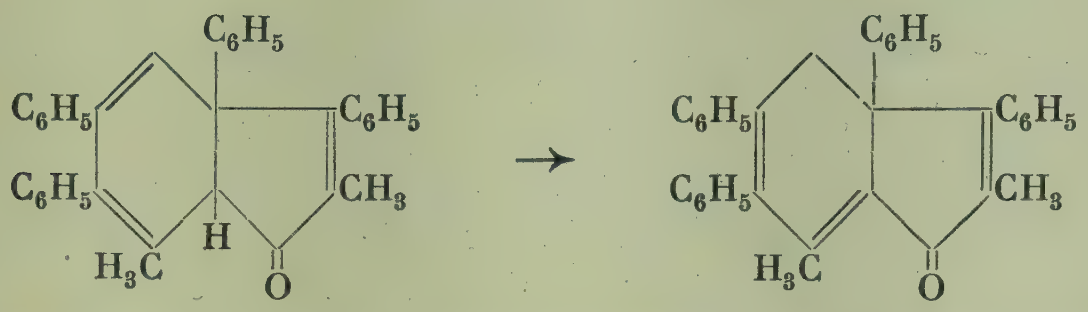
716.



$$H_2C{=}\underset{CH_3}{C}\cdot CH_2COOH \rightarrow H_3C\cdot\underset{CH_3}{C}{=}CHCOOH$$

A mixture of 3-methyl-3-butenoic acid, dry ether, and 90%-H_2SO_4 allowed to stand at room temp. for 48 hrs. → β,β-dimethylacrylic acid. Y: 97%. R. B. Wagner, Am. Soc. *71*, 3214 (1949).

717.



to conjugated double bonds. 3,3a,5,6-Tetraphenyl-2,7-dimethyl-3a,7a-dihydroindenone and a little concd. H_2SO_4 in acetic acid warmed 2 hrs. on a steam bath → 3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4-dihydroindenone. Y: 92%. C. F. H. Allen and J. A. VanAllan, J. Org. Chem. *14*, 1051 (1949).

Phenols from cyclic ketones with migration of alkyl groups ←

s. *5*, 517; s. a. Am. Soc. *73*, 364 (1951)

5-Methyl-2(3H)-thiazolethiones from 5-methylene-2-thiazolidinethiones

s. *6*, 617

Iodine *I*

cis-trans Rearrangement ←

s. *4*, 669; s. a. J. A. Elvidge et al., Soc. *1950*, 2235

Hydrochloric acid *HCl*

Chlorides from ethylene derivatives with rearrangement ←

s. *6*, 554

Palladium-carbon *Pd-C*

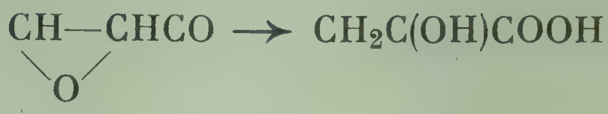
Epimerization ←

s. *6*, 838

Oxygen/Carbon Type CC ↶ OC

Sodium hydroxide *NaOH*

α-Hydroxycarboxylic acids from α,β-oxidoketones



$CH—CHCO \rightarrow CH_2C(OH)COOH$ (with O bridging CH—CH)

s. *6*, 901

Potassium hydroxide or ethyl sodium acetoacetate/pyridine ←

Baker-Venkataraman transformation ←

s. *6*, 868

Dialkylaniline *$C_6H_5NR_2$*

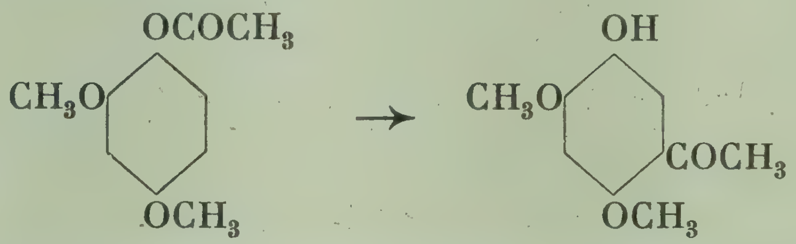
Allylphenols from allyl ethers ←
Claisen rearrangement

s. *4*, 674; s. a. Ng. Ph. Buu-Hoï, Soc. *1950*, 2096

Aluminum chloride *$AlCl_3$*

Unusual Fries rearrangement ←

718.



In a few exceptional cases, the acyl group migrates to the m-position. —E: A soln. of 1-acetoxy-2,4-dimethoxybenzene in dry nitrobenzene added with cooling to $AlCl_3$, and allowed to stand at 25° for 2 days → 2,4-dimethoxy-5-hydroxyacetophenone. Y: 50%. A. Ballio, G. *79*, 924 (1949).

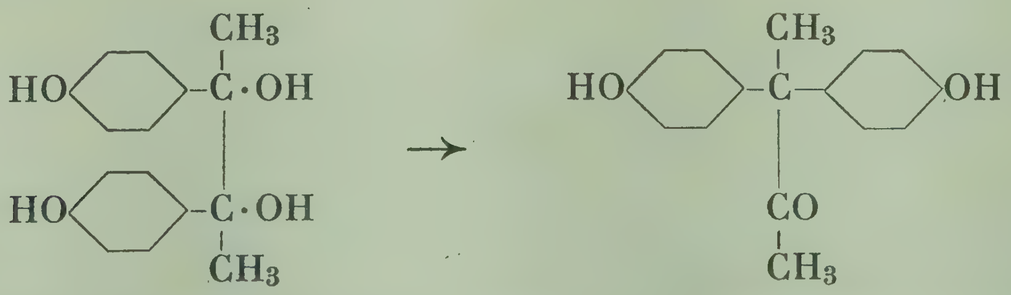
Sulfuric acid *H_2SO_4*

Rearrangement to conjugated double bonds ←

s. *2*, 624/5; s. a. E. A. Braude and C. J. Timmons, Soc. *1950*, 2007

Pinacol rearrangement ←
Deacetylation

719.

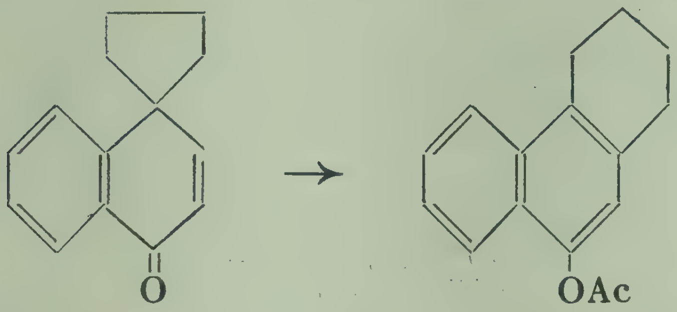


A few drops of concd. H_2SO_4 added to a suspension of 2,3-bis-(p-hydroxyphenyl)-2,3-butanediol (prepn. s. 679) in acetic anhydride, shaken until dissolved, poured on ice, and the diacetate so obtained hydrolyzed by heating with aq.-alc. KOH on a steam bath until all the alcohol has evaporated → 3,3-bis-(p-hydroxyphenyl)-2-butanone. Y: 80%. M. J. Allen, J. Org. Chem. *15*, 435 (1950); pinacol rearrangement without acetic anhydride s. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. *15*, 1191 (1950).

Phenol acetates from dienones ←

s. *3*, 597; s. a. R. B. Woodward and T. Singh, Am. Soc. *72*, 494 (1950)

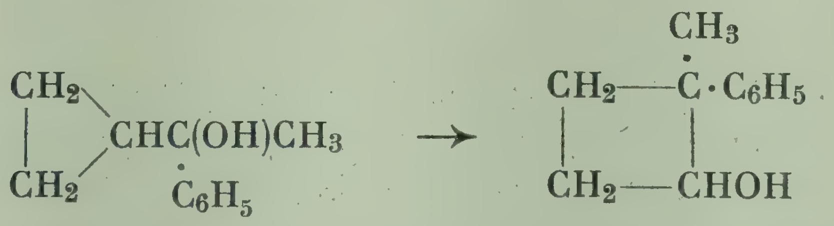
720.



Ring enlargement. A soln. of 1-keto-4,4-tetramethylene-1,4-dihydronaphthalene in acetic anhydride treated with a soln. of H_2SO_4 in acetic anhydride, and allowed to stand 4 hrs. at room temp. → 1,2,3,4-tetrahydro-9-phenanthryl acetate. Y: 95%.—The rearrangement of *spiro*-dienones represents a new method, free of inhibiting steric factors, for the preparation of rings containing 6 or more C-atoms. R. T. Arnold, J. S. Buckley, Jr., and R. M. Dodson, Am. Soc. *72*, 3153 (1950).

Cyclobutanes from cyclopropanes ←

721.



$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!CH\underset{C_6H_5}{C}(OH)CH_3 \rightarrow \begin{matrix} CH_2 - \overset{CH_3}{C} \cdot C_6H_5 \\ | \qquad\quad | \\ CH_2 - CHOH \end{matrix}$$

Methylphenylcyclopropylcarbinol boiled 5 hrs. with 25%-H_2SO_4 → 1,1-methylphenyl-2-cyclobutanol. Y: 47%. T. A. Favorskaya and Sh. A. Fridman, Ж. *20*, 581 (1950); C. A. *44*, 7784f.

Nitrogen/Nitrogen Type CC ↶ NN

Without additional reagents *w.a.r.*

Thiazoles from thiosemicarbazides with benzidine rearrangement ←

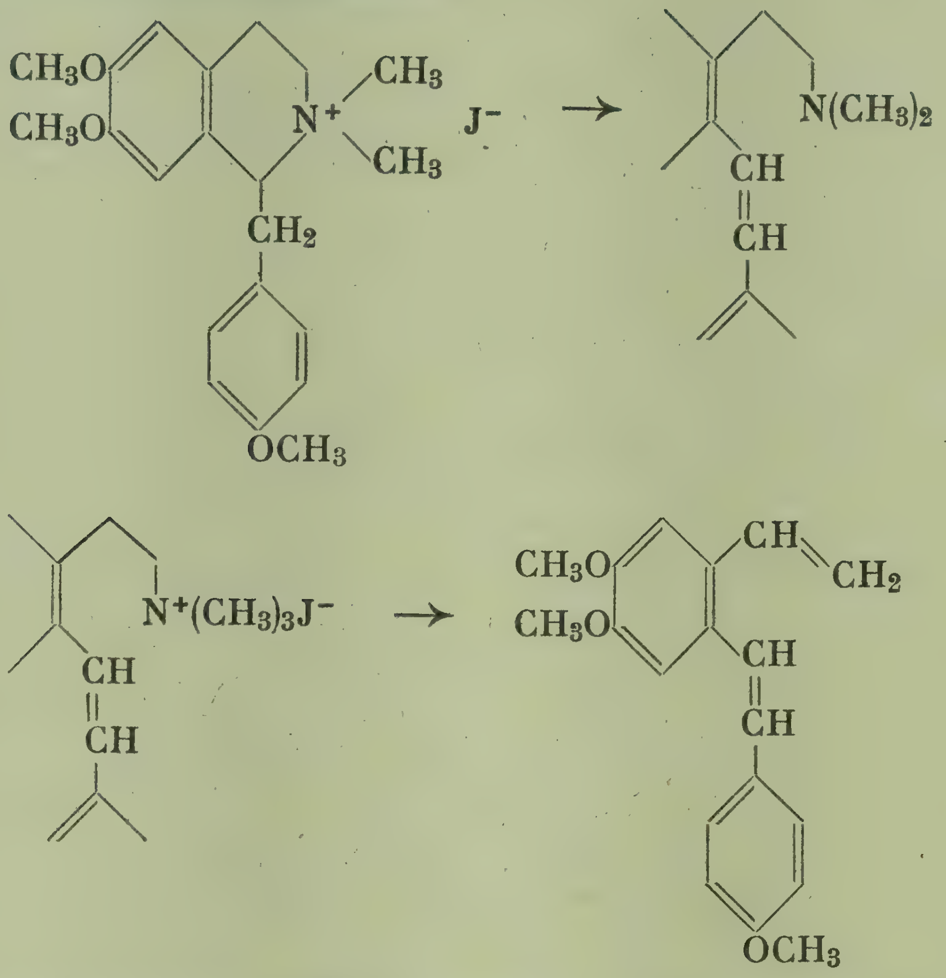
s. *6*, 646

Nitrogen/Carbon Type CC↶NC

Sodium hydroxide *NaOH*

Hofmann degradation
of quaternary ammonium salts
Ring opening
Ethylene derivatives from amines ←

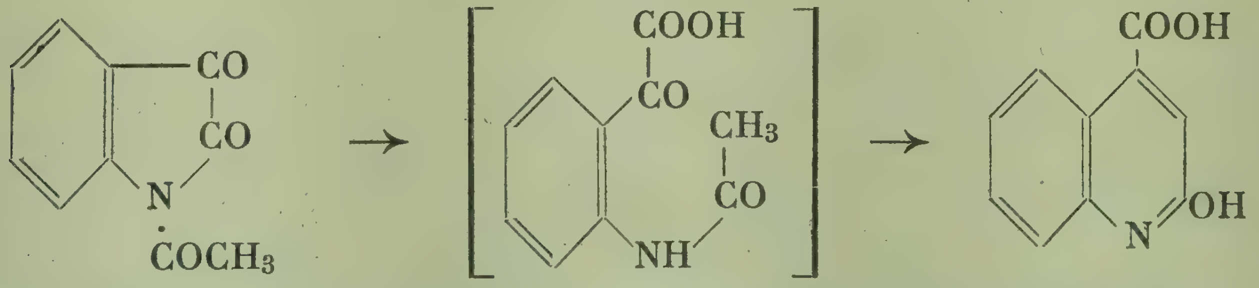
722.



O-Methyl-dl-armepavine methiodide added to methanolic NaOH, and heated on a steam bath for 90 min. → des-O,N-dimethylarmepavine (Y: ca. 100%), 90 mg. of which refluxed 90 min. with methanol and methyl iodide → 95 mg. des-O,N-dimethylarmepavine methiodide added to methanolic KOH, and heated on a steam bath for 1¾ hrs. → 4,4′,5-trimethoxy-2-vinylstilbene (Y: 95%). L. Marion, L. Lemay, and V. Portelance, J. Org. Chem. *15*, 216 (1950).

Quinoline ring from isatin ring ←

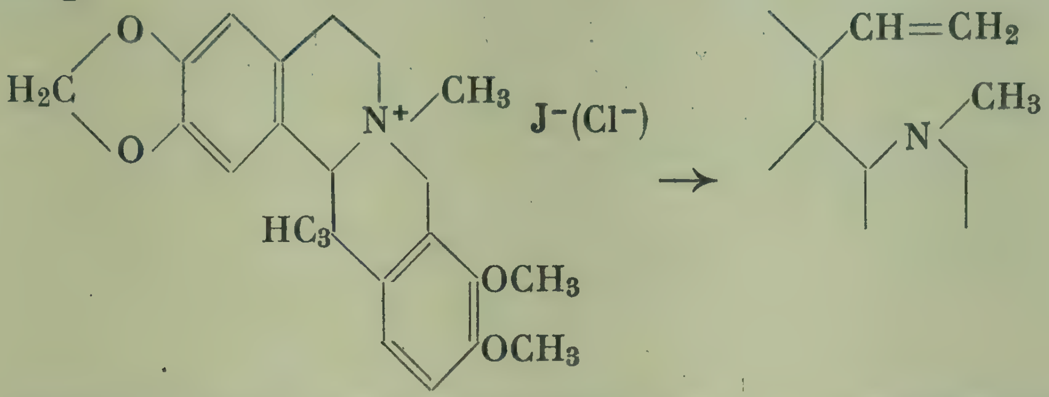
723.



N-Acetylisatin added to boiling aq. NaOH, and vigorous boiling continued for 1 hr. → 2-hydroxyquinoline-4-carboxylic acid (startg. m. f. 588). Y: 87% based on converted N-acetylisatin. J. Büchi, H. Hurni, and R. Lieberherr, Helv. *32*, 1806 (1949).

Potassium hydroxide *KOH*

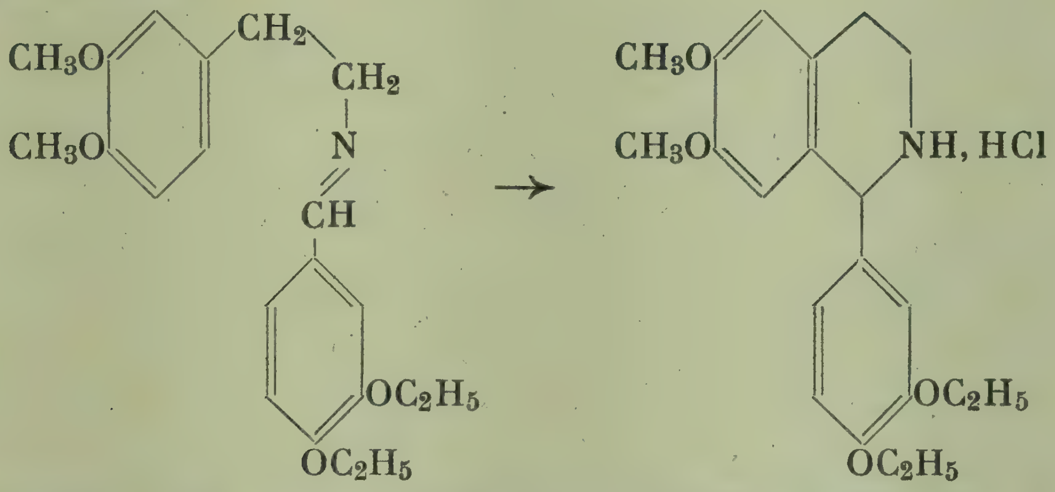
Hofmann degradation
of quaternary ammonium salts
Ring opening ←

724.


3 gm. 4-methyltetrahydroberberine methiodide converted into the methochloride with AgCl, KOH added, and concentrated until no more oil is formed → 1.5 gm. desbase.—The presence of *cis* H-atoms on the C-atoms α and β to the N is a condition for the occurrence of a smooth Hofmann degradation. F. e. s. H.-W. Bersch, Arch. Pharm. *283*, 36 (1950).

Hydrochloric acid *HCl*

1,2,3,4-Tetrahydroisoquinolines
from azomethines ○

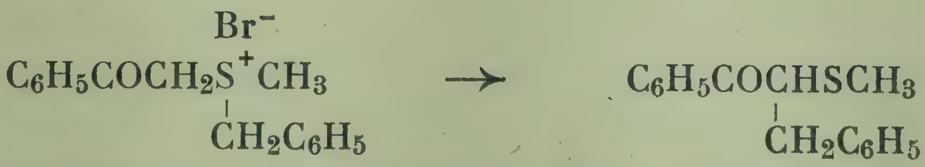
725.


24%-HCl added with vigorous stirring to N-(3,4-diethoxybenzylidene)-homoveratrylamine, and heated 40-60 min. on a water bath with continued stirring → 6,7-dimethoxy-3′,4′-diethoxy-1-phenyltetrahydroisoquinoline hydrochloride. Y: 81%. F. e. s. E. C. Weinbach and W. H. Hartung, J. Org. Chem. *15*, 676 (1950).

Sulfur/Carbon Type CC ∩ SC

Sodium/alcohol *NaOR*

Thioethers from sulfonium salts
with rearrangement ←

726.


$$\underset{CH_2C_6H_5}{C_6H_5COCH_2\overset{Br^-}{S^+}CH_3} \rightarrow \underset{CH_2C_6H_5}{C_6H_5COCHSCH_3}$$

Methyl benzyl phenacyl sulfonium bromide added to a soln. of Na in methanol, and refluxed 1 hr. on a water bath → methyl α-benzylphenacyl sulfide. Y: 81%. F. e. s. F. Krollpfeiffer and H. Hartmann, Chem. B. *83*, 90 (1950).

Carbon/Carbon Type CC ⌒ CC

Potassium/alcohol *KOR*

Carboxylic acid esters from α-halogenoketones with rearrangement ←

s. *4*, 683; s. a. Helv. *33*, 2243 (1950)

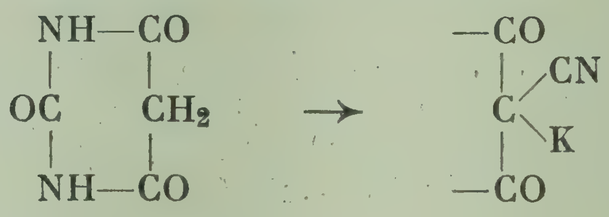
Exchange

Hydrogen ↑ CC ⇅ H

Mercuric fulminate $Hg(ONC)_2$

Replacement of hydrogen by cyano groups H → CN

727.

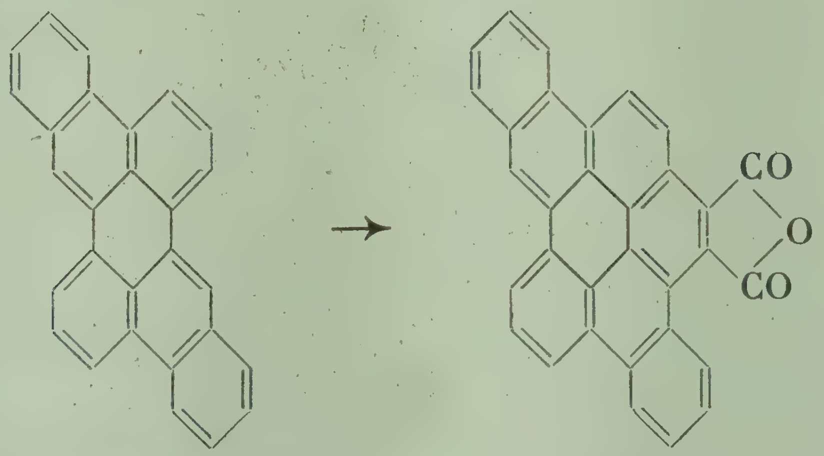


A satd. aq. soln. of 2.13 gm. barbituric acid added to a mixture of Hg(II)-fulminate and KI in water, refluxed 1.5 hrs., then treated with H_2S → 1.85 gm. K-5-cyanobarbituric acid. F. e. s. M. Ridi and G. Feroci, G. *78*, 932 (1948).

Chloranil ←

Benzene ring synthesis ○
Condensed isocyclics

728.



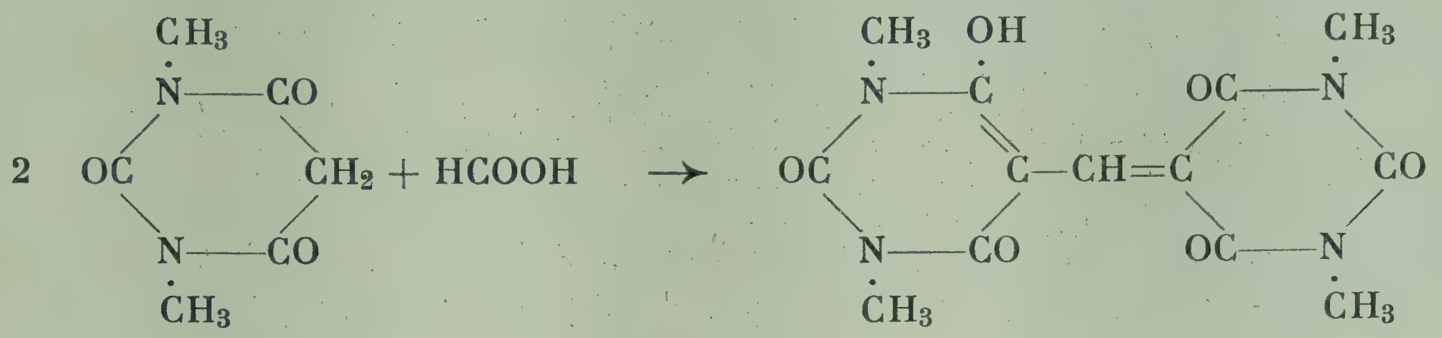
Chloranil or bromanil added portionwise to a boiling mixture of 2,3,8,9-dibenzoperylene and maleic anhydride → 1,12,2,3,8,9-tribenzoperylene-1′,2′-dicarboxylic anhydride. Y: ca. 100%. E. Clar and H. Frömmel, Chem. B. *82*, 46 (1949).

Oxygen ↑ **CC ⇅ O**

Without additional reagents *w.a.r.*

Methine condensation ·CH:

729.

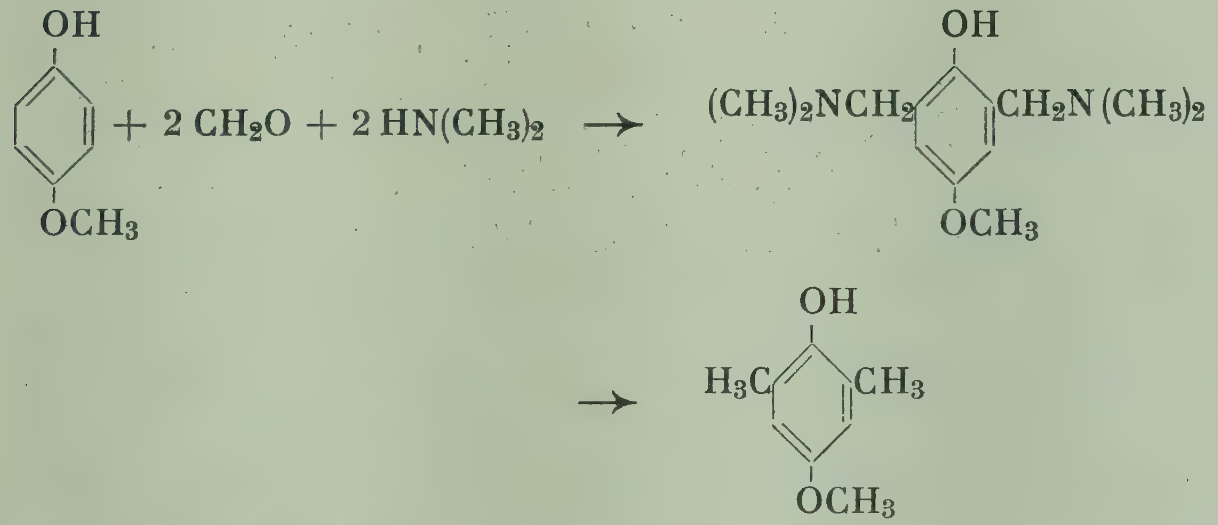


A soln. of N,N′-dimethylbarbituric acid in anhydrous formic acid heated at 120° for 20 hrs. → methinebis-(1,3-dimethylbarbituric acid). Y: 78%. F. e. s. H. Gysling and G. Schwarzenbach, Helv. *32*, 1484 (1949); s. a. M. Ridi, G. *80*, 533 (1950).

Mannich reaction
Aminomethylation H → CH_2NR_2

Replacement of hydrogen by methyl via tert. amines
Hydrogenolysis of Mannich bases

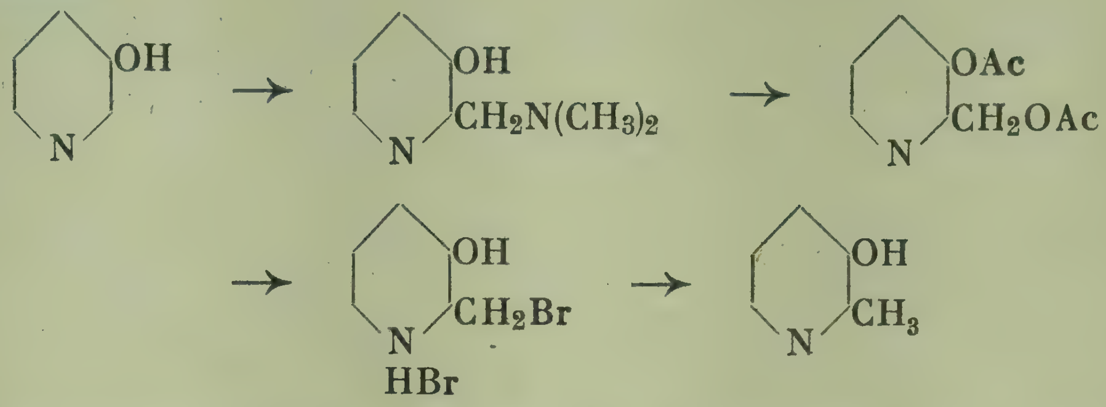
730.



37%-formaldehyde added at 15-20° over a period of 1 hr. to hydroquinone monomethyl ether and a 25% soln. of dimethylamine, stirred another hr. without cooling, then refluxed gently with stirring for 45 min., while more formaldehyde is added dropwise → 2,6-bis-(dimethylaminomethyl)-4-methoxyphenol (Crude Y: 77%) hydrogenated ca. 2 hrs. with Cu-chromite in dioxane at 235° and an initial pressure of 275 atm./room temp. → 2,6-dimethyl-4-methoxyphenol (Crude Y: 90%). W. Reeve and A. Sadle, Am. Soc. *72*, 3252 (1950); cf. R. B. Carlin and H. P. Landerl, Am. Soc. *72*, 2762 (1950); hydrogenolysis of Mannich bases s. a. Synth. Meth. *2*, 106.

Replacement of hydrogen by methyl via tert. amines, acoxy compounds and halides

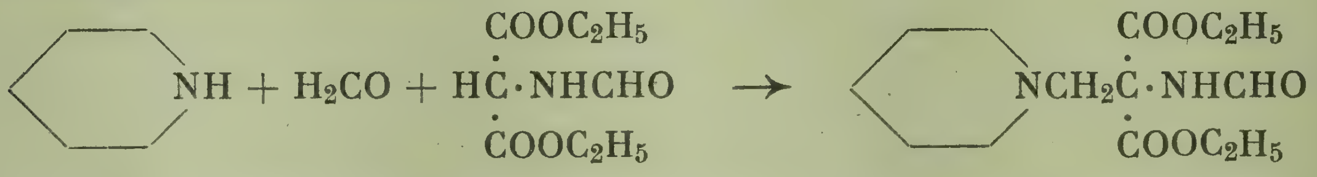
731.



35%-formalin added to an aq. soln. of 3-pyridol and dimethylamine, then heated 2 hrs. on a steam bath → 2-dimethylaminomethyl-3-pyridol (Y: 70%) refluxed 1.5 hrs. in acetic anhydride → 2-hydroxymethyl-3-pyridol diacetate dissolved in 48%-HBr, and refluxed 0.5 hr. → 2-bromomethyl-3-pyridol hydrobromide (Y: 82%) dissolved in methanol, and shaken with 3%-Pd-on-charcoal at room temp., until, after a short time, the theoretical quantity of H_2 is absorbed → 2-methyl-3-pyridol hydrobromide (Y: 90%). Overall Y: 45%. A. Stempel and E. C. Buzzi, Am. Soc. *71*, 2969 (1949); acoxy compounds from tert. amines s. a. S. R. Finn and W. G. Musty, J. Applied Chem. *1*, 182 (1951).

Mannich reaction with acylaminomalonic esters

732.



Diethyl formamidomalonate dissolved in piperidine without warming, treated with 40%-formalin, and stirred rapidly for ca. 1 min. until the mixture solidifies → diethyl (1-piperidylmethyl)formamidomalonate (startg. m. f. 789). Y: 93%. F. e. s. A. Butenandt and H. Hellmann, Z. physiol. Chem. *284*, 168 (1949).

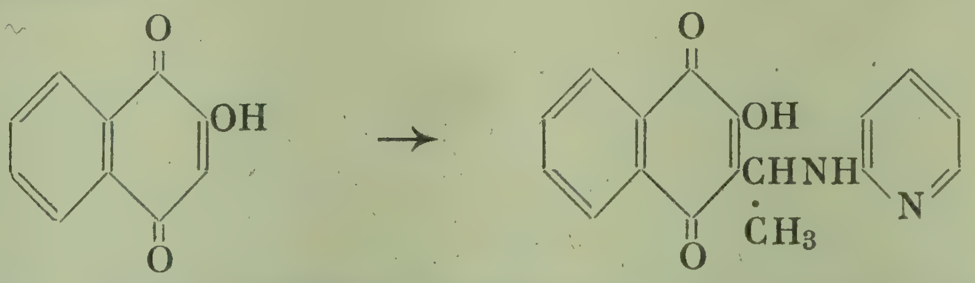
Aminomethyl-N-heterocyclics

s. *3*, 608; s. a. H. Bader, J. D. Downer, and P. Driver, Soc. *1950*, 2775.

Aminoalkylation

H → CHRNHR′

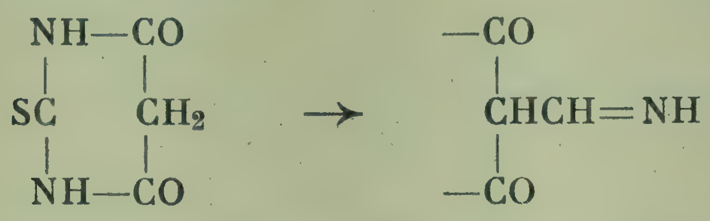
733.



Acetaldehyde added at 25-30° with shaking to a mixture of 2-hydroxy-1,4-naphthoquinone and 2-aminopyridine, then allowed to stand for ca. 24 hrs. → 2-hydroxy-3-α-(2′-pyridylamino)ethyl-1,4-naphthoquinone. Y: 96%. F. e. s. C. E. Dalgliesh, Am. Soc. *71*, 1697 (1949).

Aldimines from hydrocarbons $CH_2 \rightarrow CHCH:NH$

734.



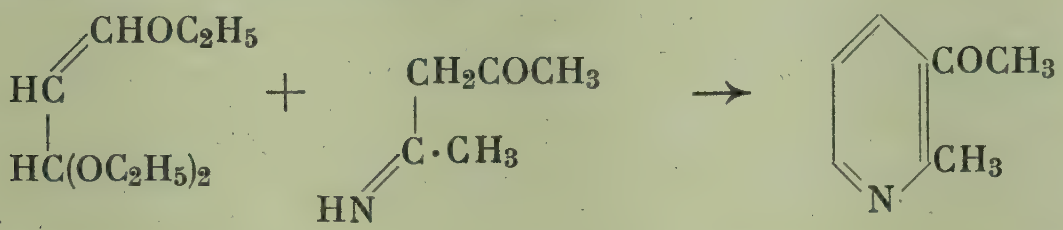
2 gm. thiobarbituric acid and NH_4-formate gradually heated to 190°, then 1 hr. at the same temp. → 2.1 gm. thiobarbituric aldimine. M. Ridi, G. *79*, 175 (1949).

4-Hydroxycoumarins ○

s. *2*, 635; improved procedure s. Bl. *1950*, 1248

Pyridine ring from enolether acetals

735.



β-Ethoxyacrolein diethylacetal and acetylacetone imine refluxed 24 hrs. at 105-110° → 2-methyl-3-acetylpyridine. Y: 90-95%. A. Dornow et al., Chem. B. *82*, 117, 216 (1949).

Lithium *Li*

Ketones from carboxylic acids COOH → COR

s. *5*, 532; cf. W. G. Dauben and E. Hoerger, Am. Soc. *73*, 1504 (1951)

Hantzsch pyridine ring synthesis

s. *1*, 542; s. a. A. P. Phillips, Am. Soc. *71*, 4003 (1949)

Sodium *Na*

Acyloins from carboxylic acid esters ←

s. *1*, 545; s. a. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, Soc. *1950*, 2743

4-Hydroxycoumarins ○

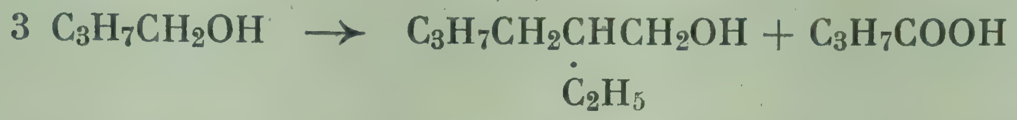
s. *4*, 698; s. a. P. Vercier, D. Molho, and C. Mentzer, Bl. *1950*, 1248

Chromone synthesis

s. *2*, 642; cf. A. Schönberg and S. Sina, Am. Soc. *72*, 3396 (1950)

Sodium/copper *Na/Cu*

Guerbet condensation of alcohols ←

736. 

$$3\ C_3H_7CH_2OH \rightarrow C_3H_7CH_2\underset{C_2H_5}{\dot{C}H}CH_2OH + C_3H_7COOH$$

148 gm. butyl alcohol, Na, and a little Cu heated in an autoclave to 300°, the pressure released to 50-60 atm., and heating continued for 6 hrs. → 79 gm. 2-ethylhexanol, 50 gm. butyric acid, and 10 gm. 2-ethylhexoic acid. F. e. s. C. Weizmann, E. Bergmann, and M. Sulzbacher, J. Org. Chem. *15*, 54 (1950); s. a. W. M. Bruner, Ind. Eng. Chem. *41*, 2860 (1949).

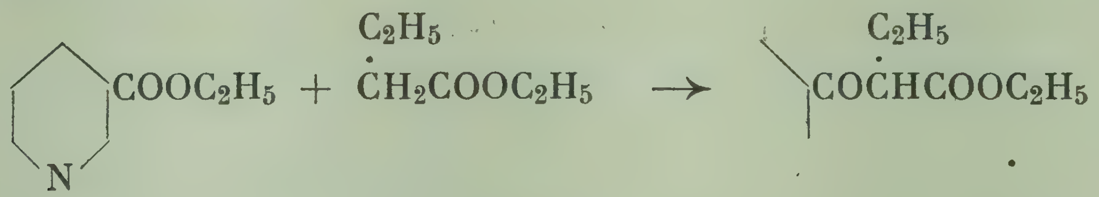
Sodium hydride **NaH**

β-Diketones COCH₂CO

737. $CH_3[CH_2]_{10}COOC_2H_5 + CH_3COCH_3 \rightarrow CH_3[CH_2]_{10}COCH_2COCH_3$

In acylations (and carbethoxylations) of ketones, NaH generally produces as good yields as $NaNH_2$ and usually better yields than Na-ethoxide or Na.—E: Acetone in dry ether added during 30-60 min. at 30-40° to a stirred mixture of ethyl laurate and NaH, and stirring continued at 40-55° with addition of more ether until at least 80% of the H_2 has been evolved → lauroylacetone. Y: 83%. F. e. s. F. W. Swamer and C. R. Hauser, Am. Soc. *72*, 1352 (1950); s. a. T. A. Geissman, Am. Soc. *71*, 1498 (1949).

β-Ketocarboxylic acid esters from carboxylic acid esters ←
Mixed ester condensation
Ball mill reactor

738. 

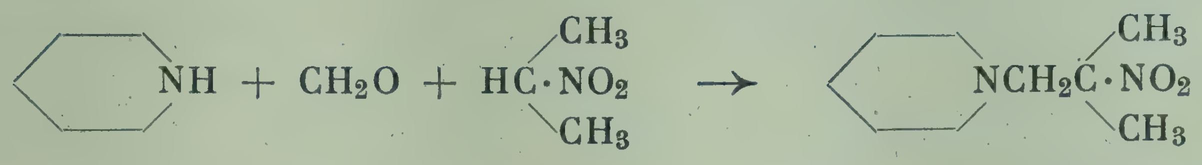
In the self-condensation of methyl and ethyl esters and especially in certain mixed ester condensations, NaH is superior to Na-ethoxide, Na, or $NaNH_2$.—The use of a ball mill reactor may be advantageous in several cases, generally resulting in higher yields in less reaction time. —E: Ethyl *n*-butyrate in dibutyl ether added dropwise at 100° over a period of 30-60 min. to a stirred mixture of ethyl nicotinate and NaH, and stirring continued at 100-110° with addition of more dibutyl ether until gas evolution stops and for 1 hr. thereafter → ethyl α-nicotinyl-*n*-butyrate. Y: 68%. F. e. s. F. W. Swamer and C. R. Hauser, Am. Soc. *72*, 1352 (1950).

Sodium hydroxide *NaOH*

Mannich reaction
Aminomethylation
Nitramines

H → CH_2NR_2

739.



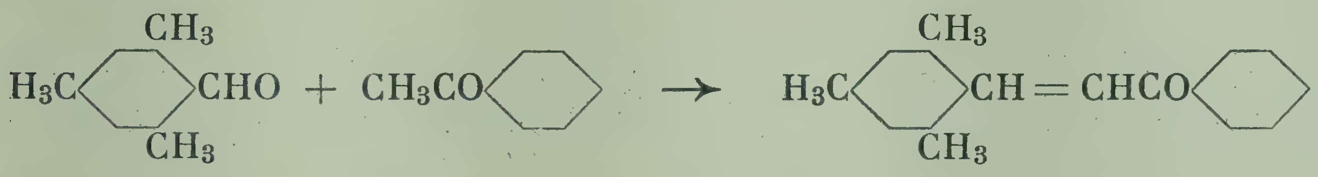
A mixture of 37%-formaldehyde and 2%-NaOH added below 10° to piperidine, 2-nitropropane, and dioxane, stirred 1 hr. after completion of the addition, then heated 1 hr. on a steam bath → N-(2-nitro-2-methylpropyl)piperidine. Y: 76.5%. F. e. s. G. B. Butler and F. N. McMillan, Am. Soc. *72*, 2978 (1950).

α,β-Ethyleneketones from aldehydes

$CHO \rightarrow CH:CHCOR$

s. *1*, 549; s. a. P. T. Mora and T. Széki, Am. Soc. *72*, 3009 (1950); K. Alexander et al., Am. Soc. *72*, 5506 (1950)

740.



Chalcones. Acetophenone added with stirring to a soln. of NaOH in ethanol, cooled to 0°, mesitaldehyde added with stirring, and, after 3 hrs., stirring continued at 15-20° for 15 hrs. → mesitalacetophenone startg. m. f. 708). Y: 87%. R. C. Fuson and H. L. Jackson, Am. Soc. *72*, 1637 (1950).

Benzene ring synthesis
2,6-Polymethylene-4-nitrophenols

○

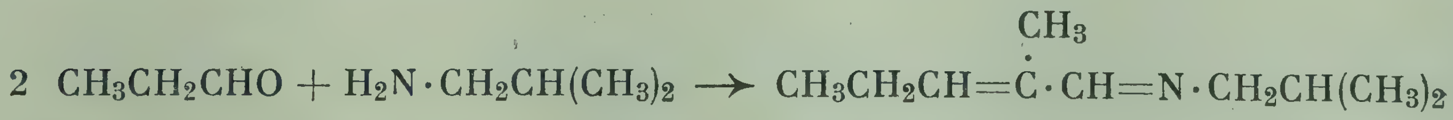
s. *4*, 701; s. a. Helv. *33*, 1937 (1950)

Potassium hydroxide *KOH*

Aldol condensation with subsequent formation of azomethines

←

741.



$$2\ CH_3CH_2CHO + H_2N\cdot CH_2CH(CH_3)_2 \rightarrow CH_3CH_2CH{=}\overset{CH_3}{\dot{C}}\cdot CH{=}N\cdot CH_2CH(CH_3)_2$$

Propionaldehyde stirred 10 hrs. at 5-8° with dil. KOH, neutralized, and isobutylamine added over a period of 1 hr. at 40-45° → 2-methyl-2-pentylideneisobutylamine (startg. m. f. 235). Y: 91%. F. e. of the reaction of aldehydes with amines s. A. M. Paquin, Chem. B. *82*, 316 (1949).

Potassium hydroxide/alcohol

Cyclopentadienones ○

s. *3*, 618; s. a. C. F. H. Allen and J. A. Van Allan, Am. Soc. *72*, 5165 (1950)

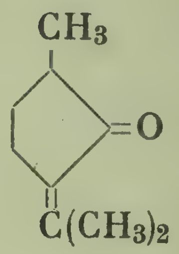
Sodium/alcohol *NaOR*

α-Hydroxymethyleneketones from ketones $CH_2 \rightarrow C{:}CHOH$

s. *2*, 643; *4*, 756; s. a. C. H. Shunk and A. L. Wilds, Am. Soc. *71*, 3946 (1949)

Synthesis of α,β-ethyleneketones from ketones ←

742.



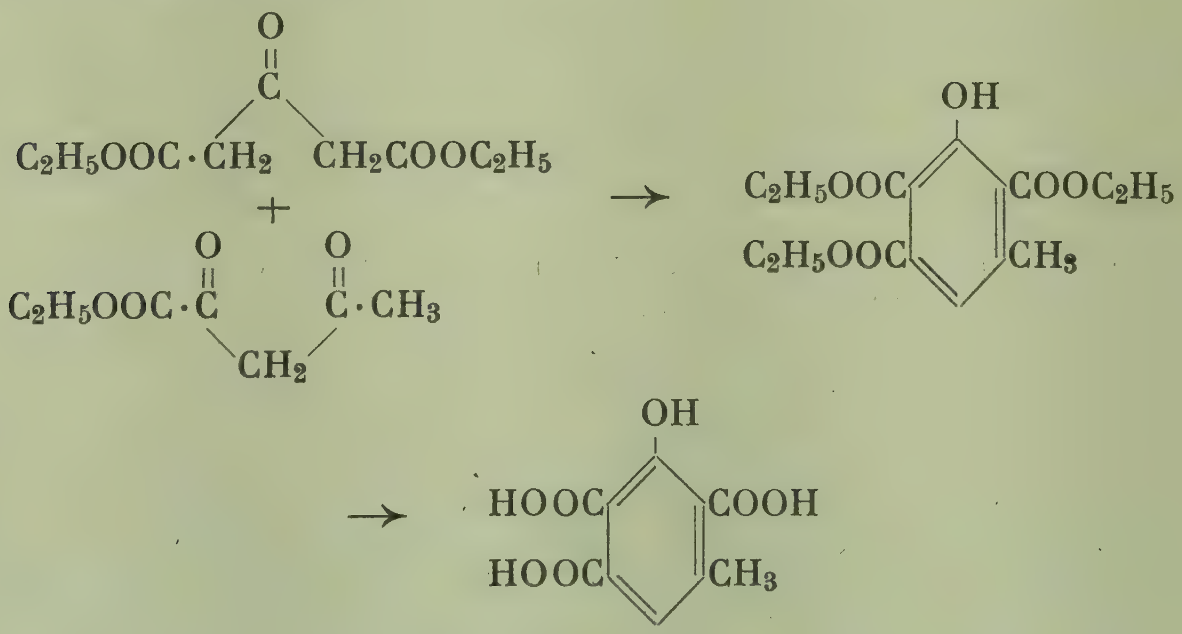
A soln. of Na in alcohol added at —10° to α-methylcyclopentanone and acetone, and allowed to stand at room temp. for 5 days → camphorone. Y: 85%. J. Golé, Bl. *1949*, 894.

α-Cyanoketones from nitriles $CH_2CN \rightarrow CH(CN)COR$

s. *2*, 645; s. a. W. R. Nes and A. Burger, Am. Soc. *72*, 5409 (1950)

Benzene ring synthesis ○

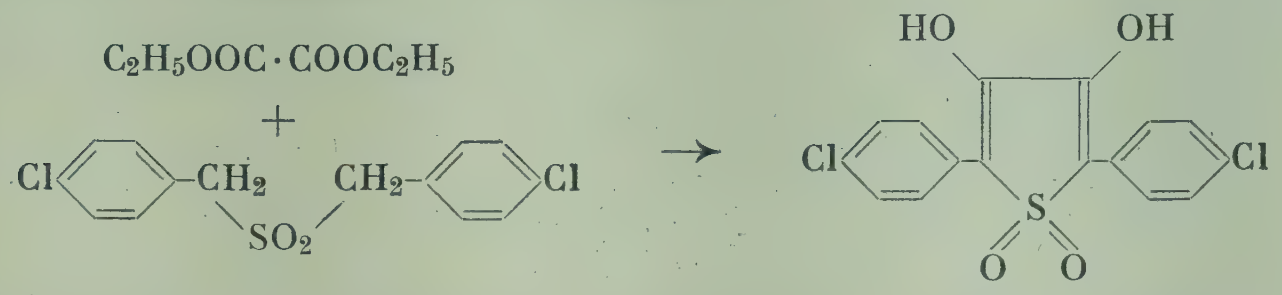
743.



Ethyl Na-acetopyruvate, obtained from ethyl oxalate, acetone, and Na in abs. alcohol according to C. S. Marvel and E. E. Dreger, Org. Synth., Coll. Vol. I, 2nd ed., p. 238, without isolation treated with diethyl acetonedicarboxylate with vigorous stirring, gently warmed until dissolved, allowed to stand in a closed flask for 48 hrs., treated with aq. KOH, the alcohol distilled off on a water bath as completely as possible, then refluxed for 2 hrs. → mono-K-isocochenillate. Y: 76%. H. Mühlemann, Pharm. Acta Helv. *24*, 351, 356 (1949).

3,4-Dihydroxythiophene 1,1-dioxides

744.



p,p′-Dichlorobenzyl sulfone and a large excess of diethyl oxalate in a soln. of Na in abs. alcohol refluxed 2 hrs. with stirring → 2,5-(p,p′-dichlorophenyl)-3,4-dihydroxythiophene 1,1-dioxide. Y: 91.1%.—The use of NaH or powdered Na gave lower yields. F. e. s. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, Am. Soc. *72*, 2856 (1950).

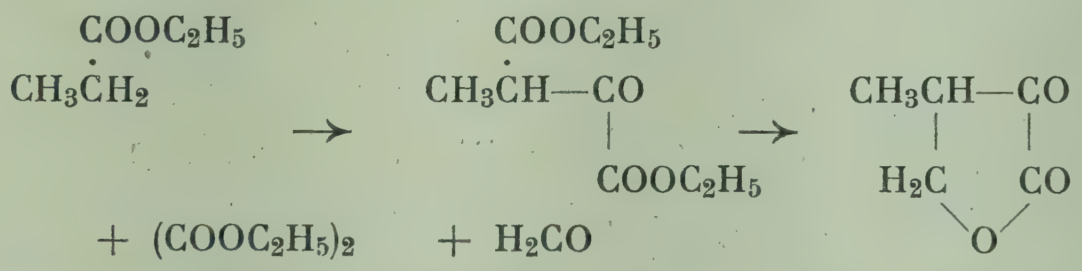
Sodium alkoxide

β-Diketones $COCH_2CO$

s. *1*, 556; with Na-methoxide s. J. C. Reid and M. Calvin, Am. Soc. *72*, 2948 (1950)

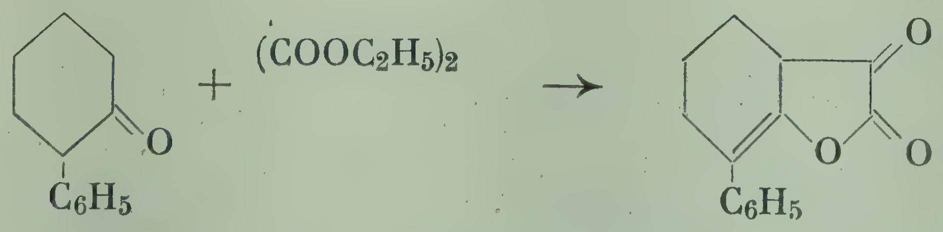
α-Keto-γ-lactones ○

745.



Simplified procedure. Diethyl oxalate, followed by ethyl propionate, added dropwise to a suspension of Na-ethoxide in abs. ether, refluxed 3 hrs., the solvent removed in vacuo, the residue dissolved in water, 35%-formalin added portionwise with water-cooling, warmed at 50° for 1 hr., the alcohol formed removed in vacuo, acidified with HCl, and refluxed 4 hrs. in the presence of hydroquinone → α-keto-β-methyl-γ-lactone. Y: 82.5%. F. e. s. F. Fleck et al., Helv. *33*, 130 (1950).

746.



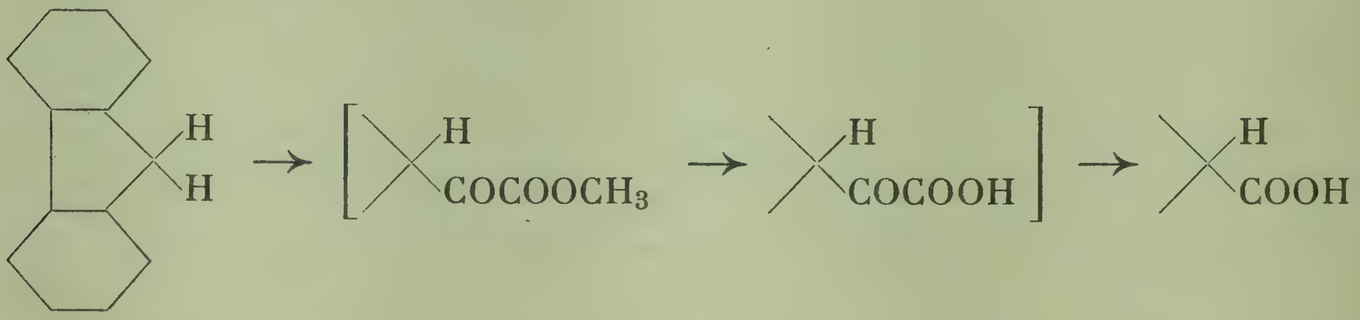
from ketones. A mixture of powdered Na-methoxide, diethyl oxalate, and benzene refluxed 10 min. with shaking, cooled, a soln. of 2-phenylcyclohexanone in benzene added, shaken for 15 min., and allowed to stand 4 hrs. at room temp. → 2-hydroxy-3-phenyl-2-cyclohexeneglyoxalic acid γ-lactone (startg. m. f. 207). Y: 79%. F. e. s. W. E. Bachmann, G. I. Fujimoto, and L. B. Wick, Am. Soc. *72*, 1995 (1950).

Potassium alkoxide (Potassium/alcohol) *KOR*

Oxalic ester synthesis H → COCOOR

Carboxylic acids from hydrocarbons via α-ketocarboxylic acid esters and α-ketocarboxylic acids Synthesis with addition of 1 C-atom

747.



Fluorene and methyl oxalate added to a soln. of K in anhydrous methanol, heated and shaken until homogeneous, methanol and excess of methyl oxalate slowly distilled off, the residue boiled 1 hr. in acetic acid-H_2SO_4-water, cooled, 30%-H_2O_2 added in portions, and allowed to stand with occasional swirling for 4 hrs. → 9-fluorenecarboxylic acid. Y: 76%. Also isolation of the intermediates s. A. Campbell and S. H. Tucker, Soc. *1949*, 2623.

α,β-Ketodicarboxylic acid esters

s. *3*, 622; *4*, 707; *6*, 858; C^{14}-compounds s. C. Heidelberger and R. B. Hurlbert, Am. Soc. *72*, 4704 (1950)

Subst., unsatd. succinic acid monoesters ←
Stobbe condensation

s. *2*, 647; s. a. W. S. Johnson and V. L. Stromberg, Am. Soc. *72*, 505 (1950); also use of NaH s. J. G. Burr, Jr., W. F. Holton, and C. N. Webb, Am. Soc. *72*, 4903 (1950); with aldehydes s. G. Tschudi and H. Schinz, Helv. *33*, 1865 (1950)

Sodium amide $NaNH_2$

α,β-Ethylenenitriles from ketones $CO + H_2\dot{C}\cdot CN \rightarrow C:\dot{C}\cdot CN$

s. *4*, 711; s. a. S. Wawzonek and E. M. Smolin, Org. Synth. *31*, 52 (1951)

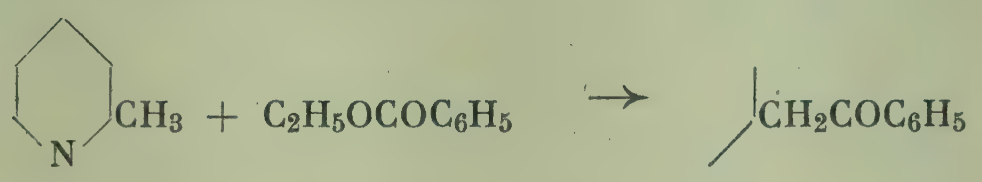
β-Diketones from carboxylic acid esters — $COCH_2CO$

s. *4*, 713; relative reactivity of the esters s. J. K. Sneed and R. Levine, Am. Soc. *72*, 5219 (1950)

Potassium amide — *KNH_2*

Ketones from carboxylic acid esters — $COOR \rightarrow COR'$

748.

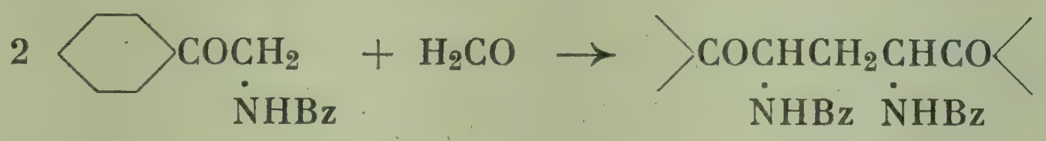


α-Picoline added with stirring during 6 min. to a KNH_2 soln. (from K, liq. NH_3, and $FeCl_3$ catalyst), ethyl benzoate added over a period of 8 min., stirred for 20 min., diluted with ether, stirring continued for 6 hrs., during which time the mixture was allowed to come to room temp., and the reaction product isolated as hydrobromide → α-phenacylpyridine hydrobromide. Y: 44%. D. R. Howton and D. R. V. Golding, J. Org. Chem. *15*, 1 (1950); also with $NaNH_2$ s. M. J. Weiss and C. R. Hauser, Am. Soc. *71*, 2023 (1949).

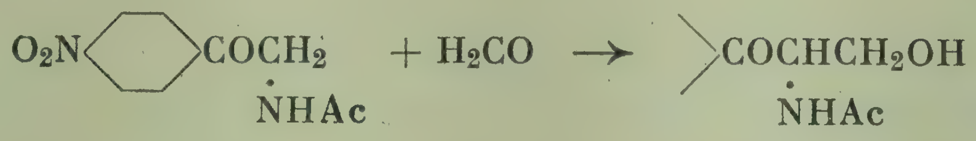
Potassium carbonate — *K_2CO_3*

Methylene bridging and hydroxymethylation ←

749.



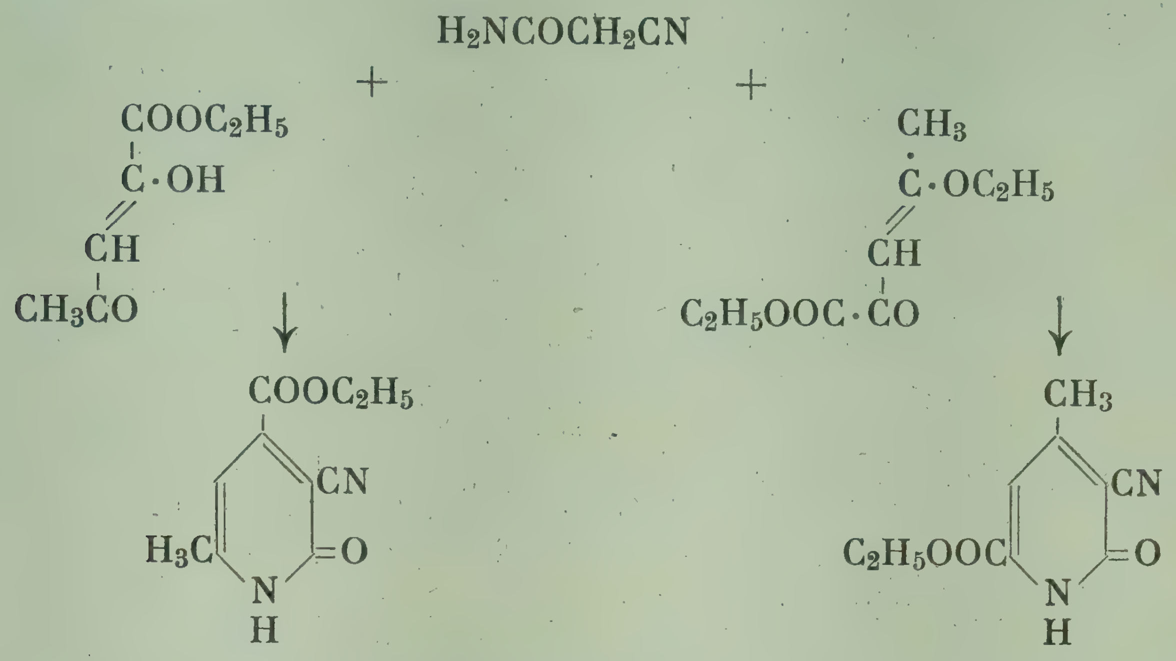
α-Benzamidoacetophenone, paraformaldehyde, K_2CO_3, and methanol shaken at room temp. for 20 min. → 1,5-diphenyl-2,4-dibenzamido-1,5-pentadione. Y: 90%. (Am. Soc. *71*, 2469.)



A mixture of p-nitro-α-acetamidoacetophenone, 95%-ethanol, excess 36-38% aq. formaldehyde, and *a small amount of $NaHCO_3$* stirred 2 hrs. at 35° → p-nitro-α-acetamido-β-hydroxypropiophenone. Y: 86%. (Am. Soc. *71*, 2473.) L. M. Long and H. D. Troutman, Am. Soc. *71*, 2469, 2473 (1949); hydroxy methylation s. a. Am. Soc. *72*, 4445 (1950); Ph. Buu-Hoï and H. Khôi, C. r. *229*, 1343 (1949); Soc. *1950*, 2766; *1951*, 255; cf. G. Carrara and G. Weitnauer, G. *81*, 142 (1951).

β-Cyanopyridones ○

750.



Anhydrous K-carbonate gradually added to a soln. of cyanoacetamide in acetone, then

acetonyloxalic ester	O-ethyl acetonyloxalic ester

dropped in with vigorous stirring, boiling and stirring continued for

6 hrs. → ethyl 2-methyl-5-cyano-6(1H)-pyridone-4-carboxylate. Y: 82.2%.	for ca. 14 hrs. → ethyl 4-methyl-5-cyano-6(1H)-pyridone-2-carboxylate. Y: 73%.

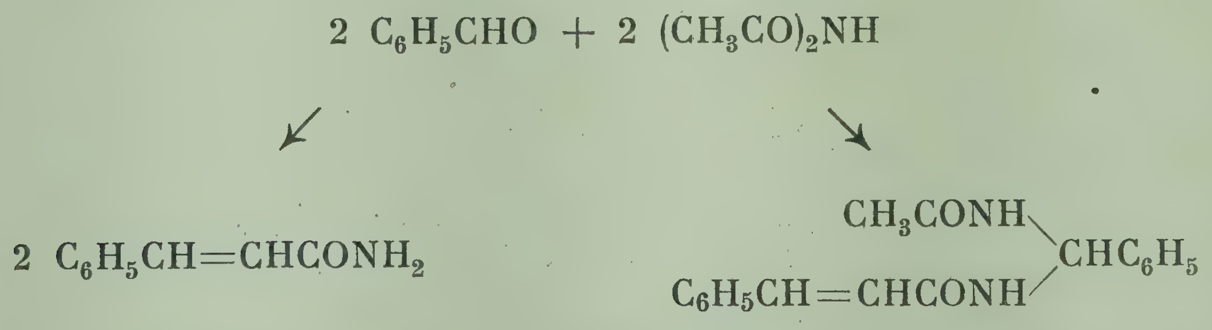
F. e.s. H. Henecka, Chem. B. *82*, 36 (1949).

Sodium acetate and potassium acetate *CH_3COONa and CH_3COOK*

α,β-Ethylenecarboxylic acid amides and unsym. 1,1-di(acylamino) compounds from aldehydes and diacylamines

Cation specificity ←

751.



$$2\ C_6H_5CHO + 2\ (CH_3CO)_2NH \rightarrow 2\ C_6H_5CH{=}CHCONH_2 \quad \text{and} \quad \begin{matrix} CH_3CONH \\ C_6H_5CH{=}CHCONH \end{matrix}\!\!>\! CHC_6H_5$$

Benzaldehyde and diacetimide heated

with fused Na-acetate at 220° for 8 hrs. → cinnamamide. Y: 81.2%.	with K-acetate at 180° for 5 hrs. → cinnamamide (Y: 37.5%) and benzylidene-N-acetyl-N'-cinnamoyldiamine (Y: 36.2%).

F. e. s. J. B. Polya and T. M. Spotswood, R. *70*, 269, 146 (1951).

Sodium cyanide *NaCN*

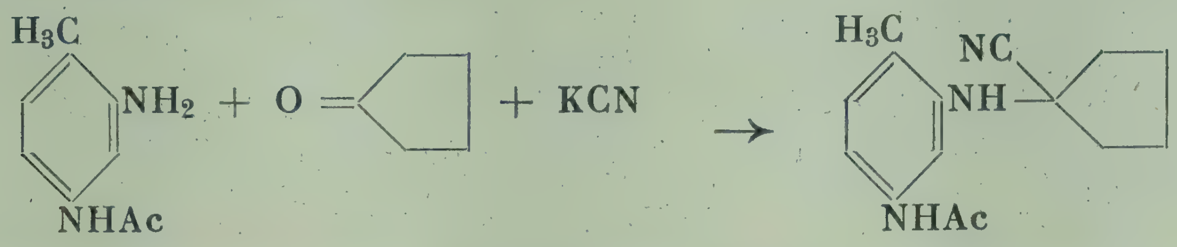
Sym. hydrazodinitriles from ketones ←

s. *6*, 869

Potassium cyanide *KCN*

α-Aminonitriles from ketones CO → C(CN)NHR

752.



p-Acetamido-o-toluidine and cyclopentanone in acetic acid treated with aq. KCN, and left at room temp. for 36 hrs. → 1-(p-acetamido-o-toluidino)-1-cyanocyclopentane. Y: 75%. F. e. s. A. E. Bond, T. Deegan, and S. G. P. Plant, Soc. *1949*, S160.

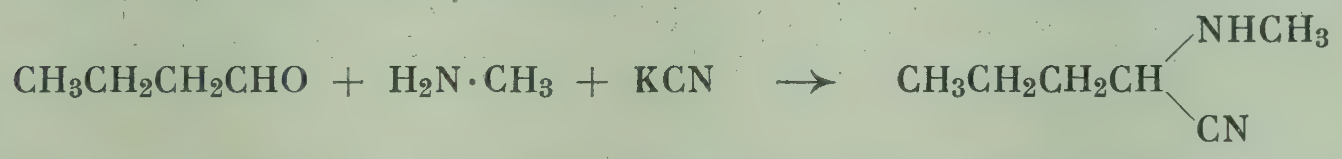
Hydantoins from oxo compounds ○

s. *4*, 715; s. a. J. Org. Chem. *15*, 901 (1950)

Sodium hydrogen sulfite *$NaHSO_3$*

α-Aminonitriles from aldehydes CHO → CH(CN)NHR

753.



$$CH_3CH_2CH_2CHO + H_2N\cdot CH_3 + KCN \rightarrow CH_3CH_2CH_2CH(NHCH_3)(CN)$$

n-Butyraldehyde added with cooling and stirring to an aq. soln. of Na-pyrosulfite ($Na_2S_2O_5$), after 30 min. 1.5 equivalents of 33% aq. methylamine run in rapidly, after a further 30 min. finely powdered KCN added, and stirring continued for 1 hr. → α-methylamino-n-valeronitrile. Y: 80%. F. e. s. A. H. Cook and S. F. Cox, Soc. *1949*, 2334.

Sodium compound ←

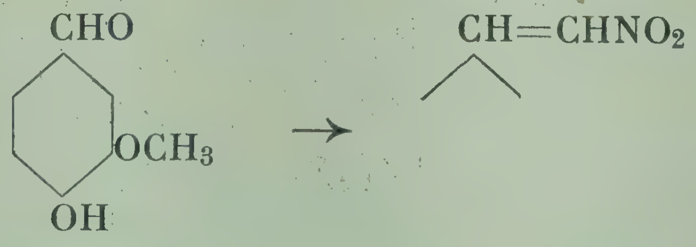
Phenol ring from β-dioxo compounds ○

s. *4*, 705; s. a. Helv. *34*, 258 (1951)

Methylamine *CH_3NH_2*

α-Nitroethylene derivatives from aldehydes CHO → CH : C·NO_2

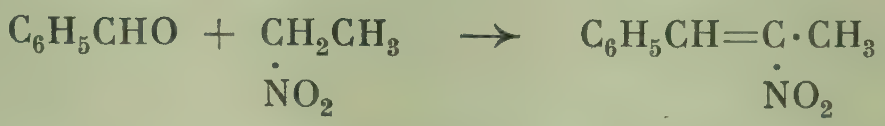
754.



A mixture of methylamine hydrochloride, Na-carbonate, and methanol stirred well, filtered, added to a soln. of vanillin and nitromethane in methanol, and kept at room temp. in the dark for 72 hrs. → 4-hydroxy-3-methoxy-β-nitrostyrene (startg. m. f. 87). Y: 81%. F. e. s. F. A. Ramirez and A. Burger, Am. Soc. *72*, 2781 (1950).

n-Butylamine *n-$C_4H_9NH_2$*

755.



$$C_6H_5CHO + \underset{NO_2}{CH_2CH_3} \rightarrow C_6H_5CH{=}\underset{NO_2}{C}\cdot CH_3$$

Benzaldehyde, nitroethane, and some n-butylamine in abs. ethanol refluxed 8 hrs. → 1-phenyl-2-nitropropene (startg. m. f. 241). Y: 86.5%, conversion 64%. F. e. s. H. B. Hass, A. G. Susie, and R. L. Heider, J. Org. Chem. *15*, 8 (1950); method, s. Knoevenagel and Walter, B. *37*, 4502 (1904); with n-amylamine s. R. T. Gilsdorf and F. F. Nord, J. Org. Chem. *15*, 807 (1950).

tert. Amines ←

α-Acylamidoketones from ←
α-aminocarboxylic acids
Dakin-West reaction

756. cf. Synth. Meth. *3*, 170.

3-Picoline and 1-methylpiperidine were found to be somewhat better catalysts than pyridine. S. Searles and G. J. Cvejanovich, Am. Soc. *72*, 3200 (1950); f. mechanism s. a. C. S. Rondestvedt, Jr., B. Manning, and S. Tabibian, Am. Soc. *72*, 3183 (1950).

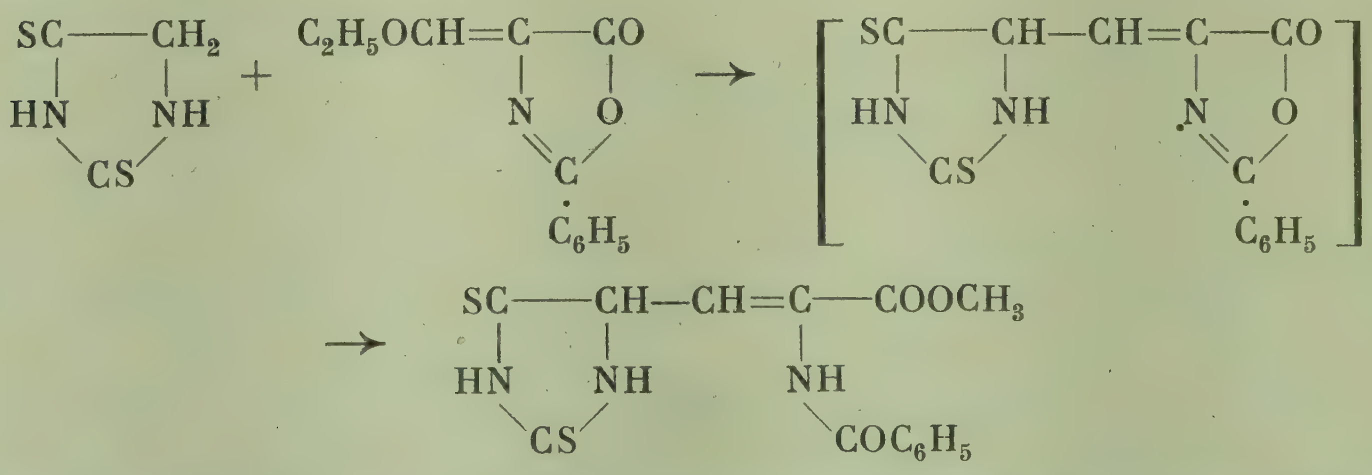
Triethylamine *$(C_2H_5)_3N$*

α,β-Ethylenecarboxylic acids from aldehydes CHO → CH:CRCOOH

s. *4*, 717; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am Soc. *73*, 1414 (1951)

Methine condensation ←
Oxazolone ring opening

757.



Dithiohydantoin and 2-phenyl-4-ethoxymethyleneoxazolone treated with methanol and triethylamine, whereupon the temp. rises almost to the boiling point, after 0.5 hr. at room temp. 2 *N* methanolic Na-methoxide added with ice-cooling, and the soln. kept at 0° for 12 hrs.

→ methyl α-benzamido-β-(2,4-dimercapto-5-glyoxalinyl)acrylate. Y: 93.5%.—The intermediate product can be isolated. F. e. s. A. C. Davis and A. L. Levy, Soc. *1949*, 2179.

Piperidine $C_5H_{11}N$

Methylene bridge with formaldehyde $2\,RH \rightarrow R\cdot CH_2\cdot R$

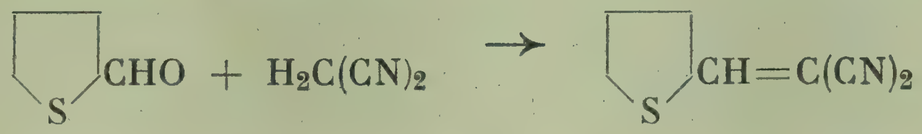
s. *4*, 720; s. a. H. B. Henbest and E. R. H. Jones, Soc. *1950*, 3628

α,β-Ethylenecarboxylic acids from aldehydes $CHO \rightarrow CH:CHCOOH$
Doebner modification of the Perkin reaction

s. *1*, 570; *2*, 657; s. a. J. Koo et al., Org. Synth. *31*, 35 (1951); M. Sulzbacher, J. Applied Chem. *1*, 95 (1951)

α,α-Ethylenedinitriles from aldehydes $CHO \rightarrow CH:C(CN)_2$

758.



A mixture of 2-thiophenealdehyde, malononitrile, and abs. ethanol heated to boiling, 2 drops of piperidine added, and heating continued for an additional 5 min. → 2-thenalmalononitrile. Y: 97%. W. S. Emerson and T. M. Patrick, Jr., J. Org. Chem. *14*, 790 (1949).

Alkylideneacetoacetic esters from aldehydes $CHO \rightarrow CH:C(COCH_3)COOR$

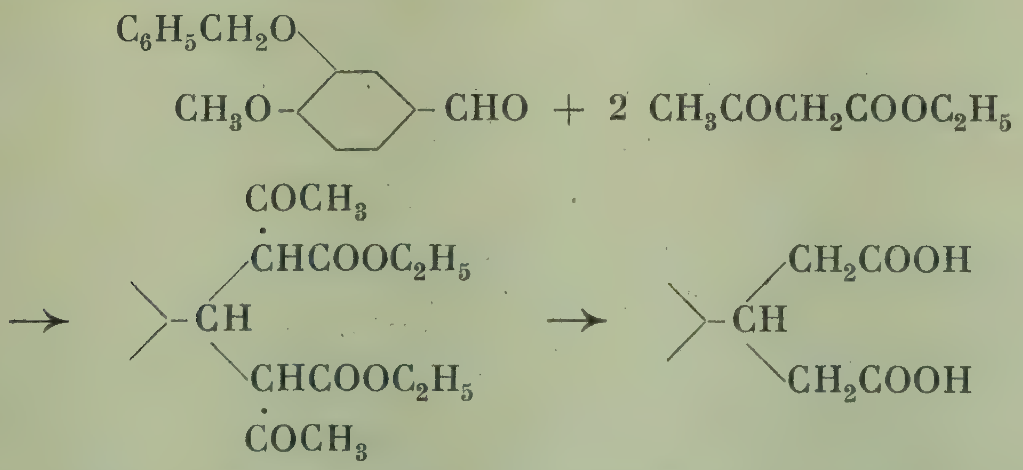
s. *1*, 400, 571; s. a. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, Soc. *1950*, 2130

α,β-Ethylene-β-dicarboxylic acid esters from aldehydes $CHO \rightarrow CH:C(COOR)_2$
Knoevenagel synthesis

s. *3*, 632; s. a. J. Jaques and A. Horeau, Bl. *1950*, 512

β-Subst. glutaric acids from aldehydes via arylmethylene-bis-acetoacetates ←

759.



A mixture of benzylisovanillin, 2 moles of ethyl acetoacetate, and piperidine in 95%-ethanol allowed to stand at room temp. for 19 hrs.

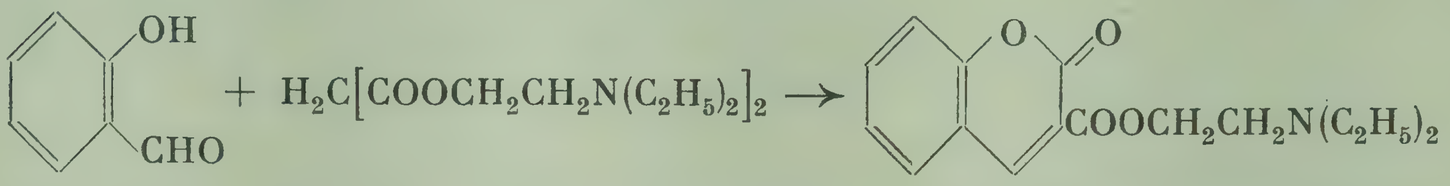
→ ethyl benzylvanillal-bis-acetoacetate (Y: 70%) refluxed vigorously for 3 hrs. in aq.-alc. NaOH → β-(3-benzoxy-4-methoxyphenyl)glutaric acid (Y: 95%). F. e. s. W. T. Smith, Jr., and P. G. Kort, Am. Soc. *72*, 1877 (1950).

Styrylheterocyclics $CHO + H_3C \rightarrow CH:CH$

s. *5*, 541; thiophene derivatives s. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, Soc. *1950*, 2130

Coumarin ring ○

760.

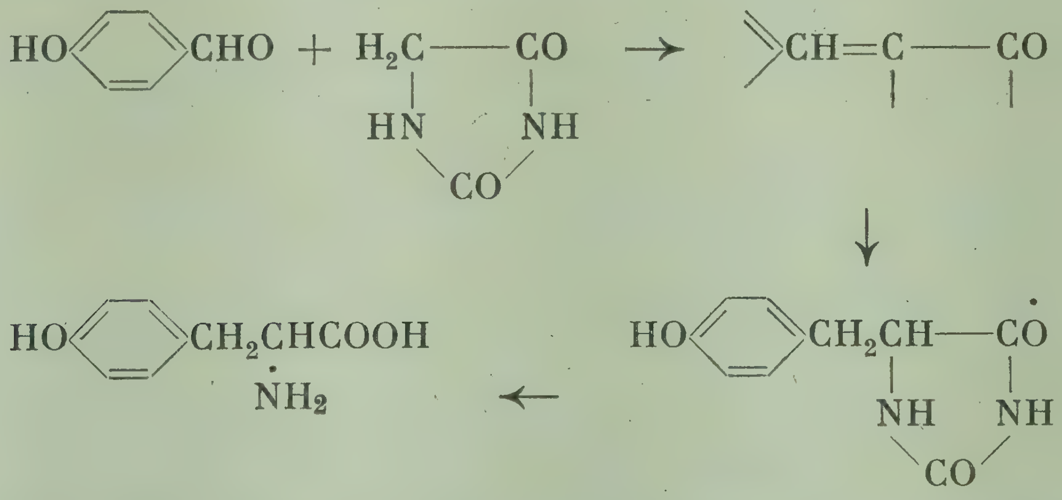


A mixture of salicylaldehyde and crude bis-(2-diethylaminoethyl)-malonate heated 3 hrs. on a steam bath in the presence of piperidine and the reaction product isolated as hydrochloride → 2-diethylaminoethyl coumarin-3-carboxylate hydrochloride. Y: excellent.—In certain cases it is necessary to force the reaction by heating and thorough use of increased amounts of piperidine catalyst. F. e. s. R. O. Clinton and S. C. Laskowski, Am. Soc. *71*, 3602 (1949); s. a. F. M. Dean, A. Robertson, and W. B. Whalley, Soc. *1950*, 895.

Morpholine ←

α-Aminocarboxylic acids from aldehydes ←
via hydantoins
Synthesis with addition of 2 C-atoms
Ethyleneheterocyclics
Hydrogenation of ethylene derivatives

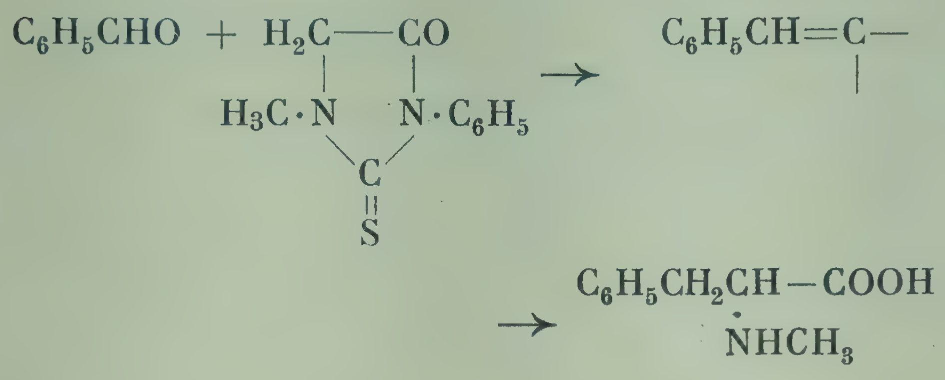
761.



Also hydrogenation of ethylene derivatives. Hydantoin, p-hydroxybenzaldehyde, and morpholine in glycerol heated 3.5 hrs. at 160° → 5-(4′-hydroxybenzylidene)hydantoin (Y: 80%) hydrogenated in alcohol with Raney-Ni at 130° and 50 atm. for 5 hrs. until absorption ceases → 5-(4′-hydroxybenzyl)hydantoin (Y: 94%) refluxed with 2 *N* NaOH for 24 hrs. → DL-tyrosine (Y: 84%). E. F. Borrows, J. C. Clayton, and B. A. Hems, Soc. *1949*, S185.

Morpholine/pyridine ←

762.

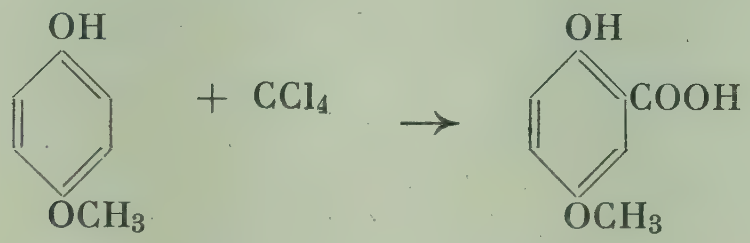


2-Thio-3-phenyl-1-methylhydantoin in pyridine containing morpholine and benzaldehyde refluxed 1 hr. → 2-thio-3-phenyl-5-benzylidene-1-methylhydantoin (Y: 92%) dissolved in acetic acid containing red P, and refluxed 5 hrs. → 2-thio-3-phenyl-5-benzyl-1-methylhydantoin (Y: 90%) refluxed 24 hrs. with aq.-alc. NaOH → β-phenyl-N-methylalanine (Y: 82%).—Morpholine in pyridine is more effective as condensing agent than Na-acetate in acetic acid.—Other heterocyclic intermediates may be preferred in some cases for sterical or other reasons. F. e. s. A. H. Cook and S. F. Cox, Soc. *1949*, 2342.

Copper *Cu*

Introduction of carboxylic acid groups into ar. rings H → COOH

763.



A mixture of hydroquinone monomethyl ether, CCl_4, 50% aq. NaOH, and Cu-powder refluxed 8 hrs. with stirring → 2-hydroxy-5-methoxybenzoic acid. Y: 74%. F. J. Villani and J. Lang, Am. Soc. *72*, 2301 (1950).

Magnesium *Mg*

Synthesis of α,β-ethylenealcohols and dienes from α,β-ethylenealdehydes ←

764.

$$\begin{tikzcd}
 & C_6H_5CH{=}CHCHO \arrow[dl] \arrow[dr] & \\
C_6H_5CH{=}CHCH(OH)CH_3 & & C_6H_5CH{=}CHCH{=}CH_2
\end{tikzcd}$$

A soln. of cinnamaldehyde in abs. ether added below 10^0 with the passage of a slow N_2-stream to a 1.5-2 *N* ethereal soln. of methyl-MgBr,

stirred 30 min., a satd. soln. of NH_4Cl (neutralized to litmus with concd. aq. NH_3) added dropwise at 5-10° over a period of 1-1.5 hrs. → *trans*-methylstyrylcarbinol. Y: 88-90%.

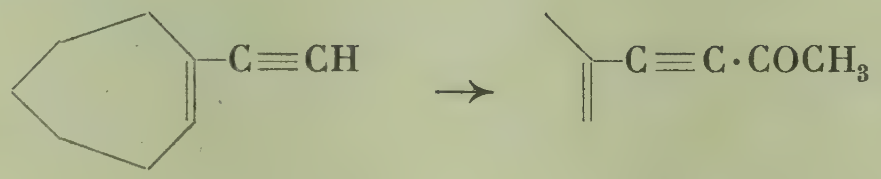
this mixture added rapidly during 5-7 min. with efficient stirring to 30%-H_2SO_4, gentle refluxing continued, and worked up after 20 min., using phenyl-β-naphtylamine as a polymerization inhibitor → *trans*-1-phenyl-1,3-butadiene. Y: 72-75%.

O. Grummitt and E. I. Becker, Org. Synth. *30,* 75 (1950).

Ketones from carboxylic acid anhydrides C⋮C′COR

Acetylene ketones

765.

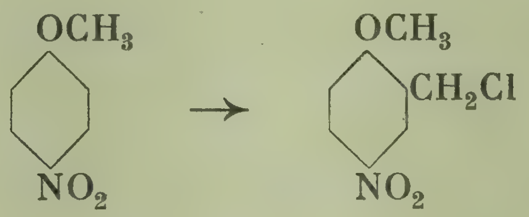


1-Ethynylcycloheptene in ether added dropwise to an ethereal soln. of ethyl-MgCl, refluxed for 2 hrs., the cooled suspension slowly added with stirring to a soln. of acetic anhydride in dry ether at — 60°, stirred for 1 hr., then the temp. allowed to rise to 20° during 2 hrs. → 4-(1-cyclohepten-1-yl)-3-butyn-2-one. Y: 70%. F. e. s. I. Heilbron et al., Soc. *1949*, 1827.

Zinc chloride *$ZnCl_2$*

Chloromethylation H → CH_2Cl

766.



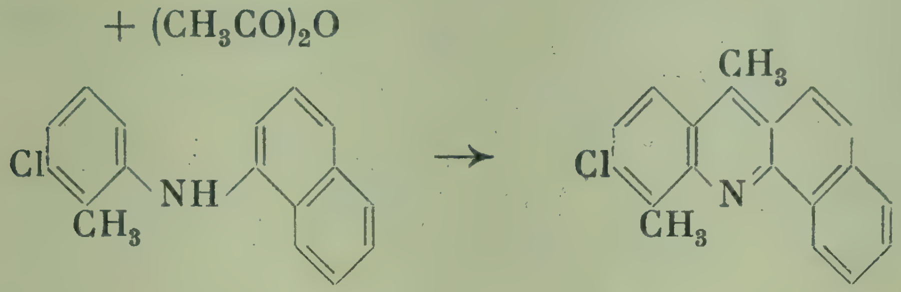
A mixture of p-nitroanisole, di(chloromethyl) ether, $ZnCl_2$, and CS_2 refluxed 9 hrs. → 4-nitro-2-chloromethylanisole. Y: 74%.—The procedure using paraformaldehyde and HCl gave a poor yield. G. Bendz et al., Soc. *1950*, 1130.

Ketones from carboxylic acid anhydrides CO·O·OC → COR

s. *3,* 651; s. a. H. Burton and P. F. G. Praill, Soc. *1951*, 726

Acridine ring ○
Modified Bernthsen reaction

67.

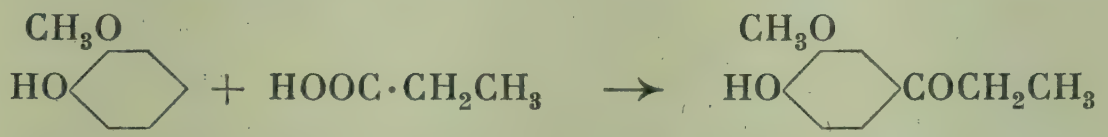


4 gm. N-(3-chloro-2-methylphenyl)-α-naphthylamine heated with acetic anhydride and $ZnCl_2$ at 190-200° for 20 hrs. → 3.5 gm. 10-chloro-7,11-dimethylbenz[c]acridine. F. e., also with acids in place of anhydrides, s. Ng. Ph. Buu-Hoï, Soc. *1950*, 1146.

Boron fluoride *BF_3*

Ketones from carboxylic acids COOH → COR

68.



A soln. of guaiacol in propionic acid saturated with BF_3 while cooling with ice, after 5 hrs. heated at 70° for 90 min. in a water-bath, then poured with stirring into aq. Na-acetate → 3-methoxy-4-hydroxypropiophenone. Y: 77.4%. G. Fodor, J. Kiss, and M. Szekerke, J. Org. Chem. *15*, 227 (1950); s. a. G. Fawaz and L. F. Fieser, Am. Soc. *72*, 996 (1950).

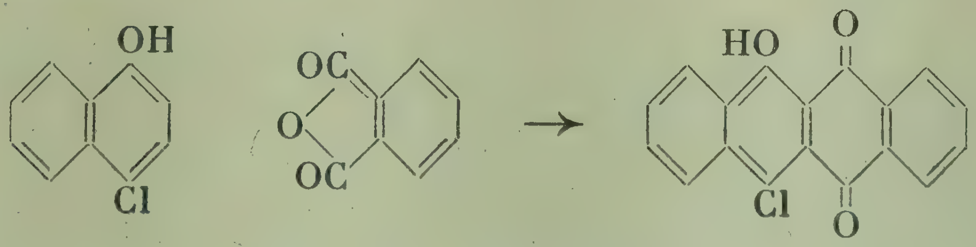
Ketones from carboxylic acid anhydrides CO·O·OC → COR

s. *4*, 725; furan- and thiophene derivatives s. a. M. W. Farrar and R. Levine, Am. Soc. *72*, 3695, 4433 (1950)

Aluminum chloride/sodium chloride *$AlCl_3/NaCl$*

Annulization ○
Hydroxyquinones

69.



A mixture of phthalic anhydride and 4-chloro-1-hydroxynaphthalene added at 150° to an $AlCl_3$-NaCl melt, and heated 2 hrs. at 210° → 4-chloro-1-hydroxy-2,3-benzanthraquinone. Y: 90%. F. e. s. H. Waldmann and E. Ulsperger, Chem. B. *83*, 178 (1950); s. a. A. M. Lukin and K. K. Mozgova, Ж. *20*, 1504 (1950); C. A. *45*, 2460c.

Ammonium acetate *CH_3COONH_4*

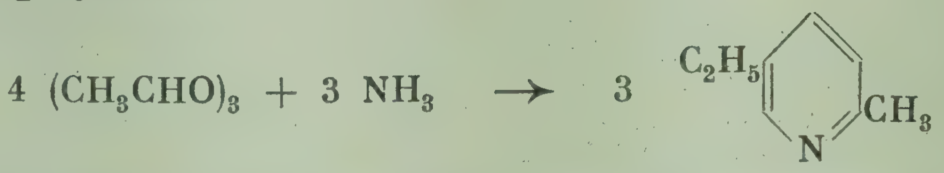
Alkylidene-cyanoacetic and -malonic esters ←

s. *1*, 586; s. a. S. M. McElvain and R. E. Lyle, Jr., Am. Soc. *72*, 384 (1950)

770. **Alkylidenecyanoacetic esters.** NH_4-acetate was found to be a satisfactory catalyst for the condensation of diaryl ketones and certain hindered ketones with ethyl cyanoacetate. The yields of alkylidenecyanoacetates were improved by the portionwise addition of the NH_4-acetate to prevent its conversion into the ineffective acetamide. E. s. E. J. Cragoe, Jr., C. M. Robb, and J. M. Sprague, J. Org. Chem. *15*, 381 (1950).

Pyridine ring synthesis ○

771.

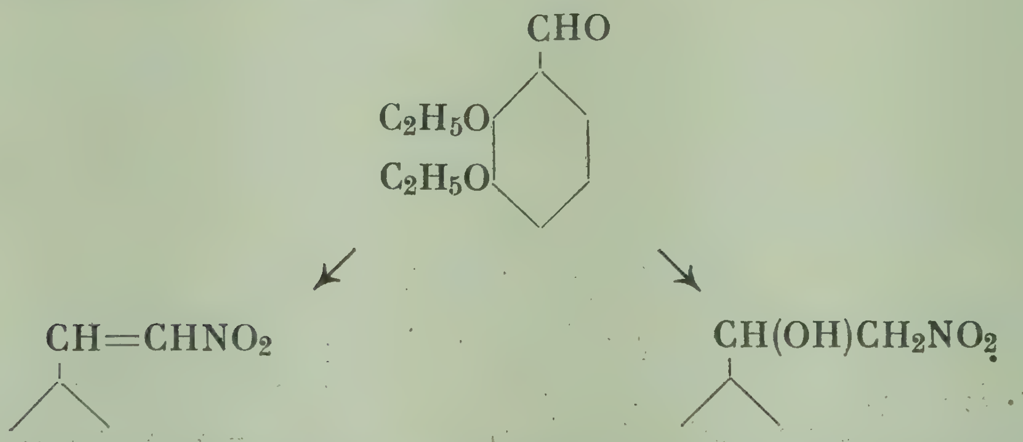


Paraldehyde, 28% aq. NH_3, and NH_4-acetate heated in an autoclave to 230° with continuous agitation, and maintained at this temp. for 1 hr. → 5-ethyl-2-methylpyridine. Y: 50-70% depending on the ratio NH_3: paraldehyde. R. L. Frank, F. J. Pilgrim, and E. F. Riener, Org. Synth. *30*, 41 (1950).

Benzylamine/acetic acid *$C_6H_5CH_2NH_2/CH_3COOH$*

α-Nitroethylene derivatives and α-nitroalcohols from aldehydes ←

772.



To a soln. of 2,3-diethoxybenzaldehyde and nitromethane in alcohol added

benzylamine and glacial acetic acid, then warmed at 50° with stirring for 10 hrs. → 2,3-diethoxy-ω-nitrostyrene. Y: 86.8%,

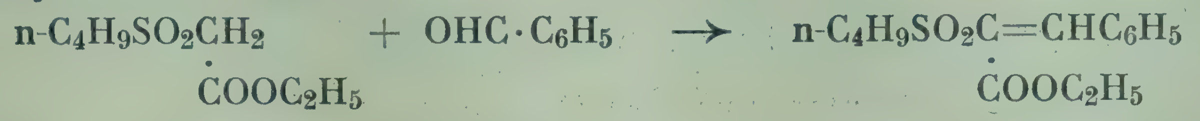
aq.-alc. KOH in small portions below 0°, and the soln. of the salt of the pseudoacid so obtained added in small portions with stirring to ice-cooled 50%-acetic acid → 2-(2,3-diethoxyphenyl)-2-hydroxy-1-nitroethane. Y: 92.8%.

F. nitroethylene derivatives s. G. Tsatsas, Bl. *1949*, 884.

Piperidinium acetate ←

α,β-Ethylenesulfones $C{:}C\cdot S_2OR$

773.



$$n\text{-}C_4H_9SO_2\underset{COOC_2H_5}{CH_2} + OHC\cdot C_6H_5 \rightarrow n\text{-}C_4H_9SO_2\underset{COOC_2H_5}{C}{=}CHC_6H_5$$

A mixture of ethyl n-butylsulfonylacetate, benzaldehyde, benzene, piperidine, and acetic acid refluxed 2 hrs. with separation of the water formed → α-n-butylsulfonyl-α-carbethoxy-β-phenylethylene. Y: 83%. F. e. s. S. Chodroff and W. F. Whitmore, Am. Soc. *72*, 1073 (1950)

Acetic anhydride *$(CH_3CO)_2O$*

Styrylheterocyclics $CHO + H_3C \rightarrow CH{:}CH$

s. *6*, 135

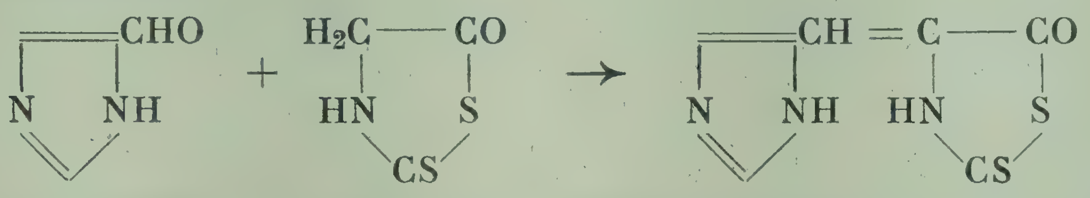
Acetic acid *CH_3COOH*

Aminomethylation
Mannich reaction $H \rightarrow CH_2NR_2$

s. *2*, 670; s. a. H. Hellmann, Z. physiol. Chem. *284*, 163 (1949)

Oxo condensation ←

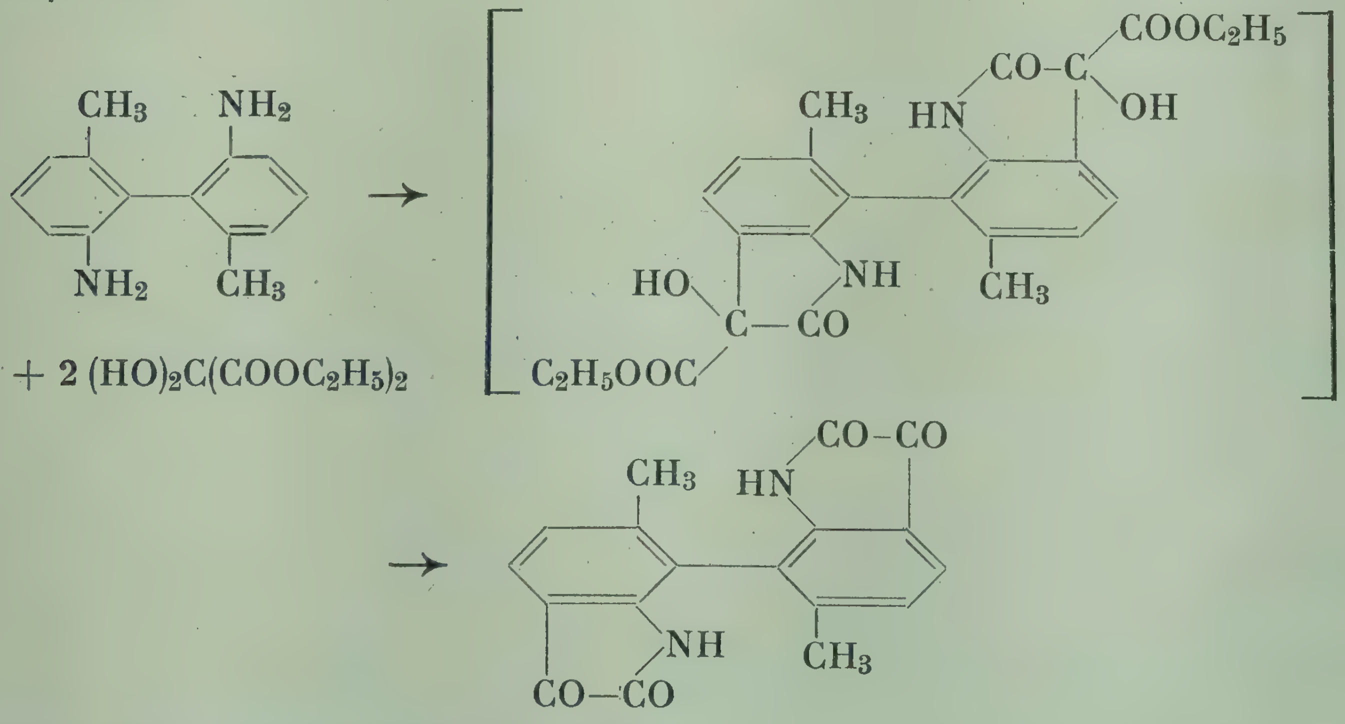
774.



2-Mercapto-5(4H)-thiazolone and 4(5)-formylglyoxaline dissolved in glacial acetic acid, heated to boiling, which maintains itself for several min. by the exothermic reaction → 2-mercapto-4-(5′-glyoxalinylmethylene)thiazol-5-one. Y: 80%. A. C. Davis, A. L. Levy, and G. F. Woods, Soc. *1949*, 2179.

Isatin ring ○

775.



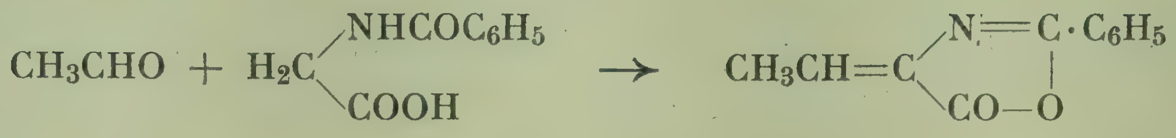
6,6′-Diamino-2,2′-dimethyl-1,1-biphenyl in boiling glacial acetic acid treated with mesoxalic ester hydrate in glacial acetic acid, heated 1 hr.

more, steam-distilled, and the residual diethyl bis(dioxindolecarboxylate) heated 2-3 hrs. in 3%-NaOH on a water bath, while air is being passed through → 6,6′-dimethyl-7,7′-biisatin. Y: 90%. W. Dethloff and H. Mix, Chem. B. *82*, 534 (1949); method, see M. J. Martinet, A. ch. [9] *11*, 15 (1949).

Lead acetate *$(CH_3COO)_2Pb$*

4-Alkylideneoxazol-5-ones

776.

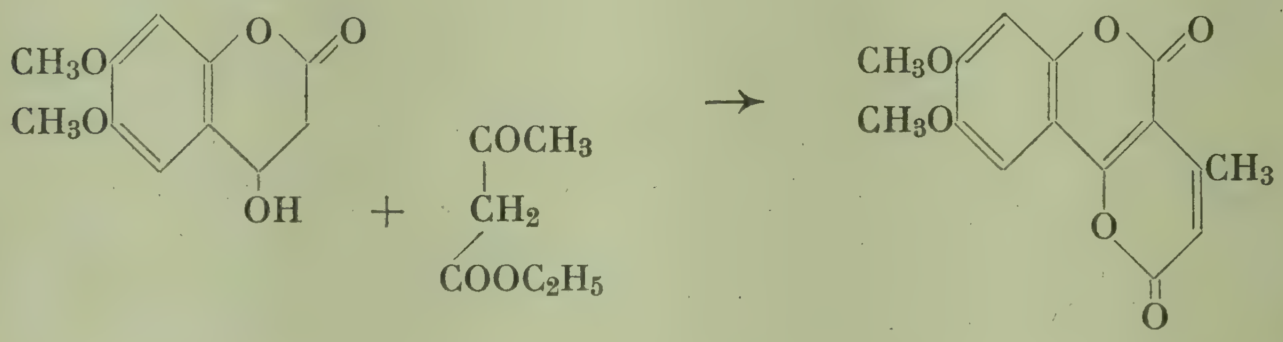


Acetic anhydride, hippuric acid, and Pb-acetate (or basic Pb-acetate) added successively to acetaldehyde, shaken at room temp. for 15 hrs., and kept for a further 33 hrs. with occasional shaking → 2-phenyl-4-ethylideneoxazol-5-one. Y: 58%.—Other catalysts gave lower yields. F. e. s. I. L. Finar and D. D. Libman, Soc. *1949*, 2726.

Phosphorus pentoxide *P_2O_5*

α-Pyrono(5′,6′,3,4)coumarins

777.



A mixture of 1 gm. 4-hydroxy-6,7-dimethoxycoumarin, P_2O_5, ethyl acetoacetate, and acetic acid heated 20 min. on a steam bath → 0.9 gm. 6,7-dimethoxy-4′-methyl-α-pyrono(5′,6′,3,4)coumarin.—$POCl_3$ gave a yield of only 0.35 gm., and concd. H_2SO_4 gave a very small amount. G. G. Badcock et al., Soc. *1950*, 903.

Phosphoric acid *H_3PO_4*

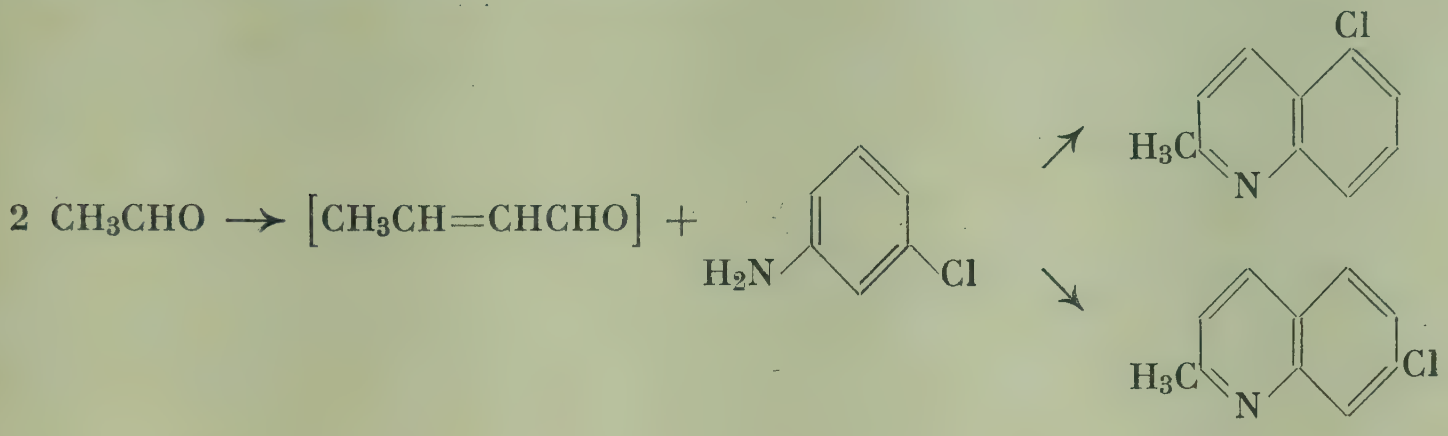
Alkylation of isocyclics with alcohols ArH → ArR

s. *3*, 643; naphthol derivatives s. Ng. Ph. Buu-Hoï, H. Le Bihan, and F. Binon, J. Org. Chem. *16*, 185 (1951)

Na-m-nitrobenzenesulfonate ←

Quinolines
Modified Döbner-Miller synthesis

778.



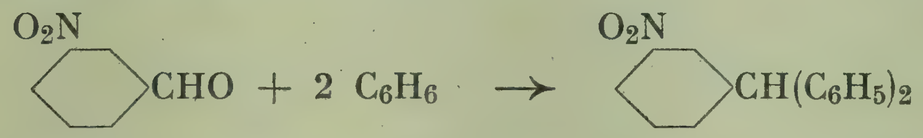
Paraldehyde added dropwise with stirring at 120-130° to m-chloroaniline, 60%-H_2SO_4, and Na-m-nitrobenzenesulfonate, stirring and refluxing continued for 1.5 hrs., and worked up, whereby any unchanged m-chloroaniline is decomposed by boiling 0.5 hr. with excess $NaNO_2$ → mixture consisting of ca. 75% 7- and 25% 5-chloroquinaldine. Y: 60%.—The proportion of 7-subst. isomer increases with decrease of acid concentration. A. M. Spivey and F. H. S. Curd, Soc. *1949*, 2656.

Sulfuric acid *H_2SO_4*

Triarylmethanes from arylaldehydes

CHO → CHR_2

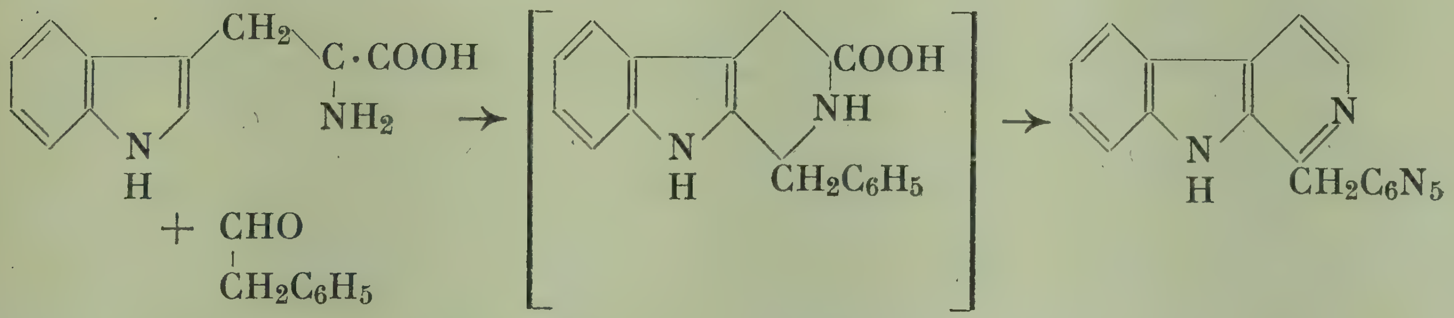
779.



A mixture of n-nitrobenzaldehyde, concd. H_2SO_4, and benzene shaken at 25° for 24 hrs. in a closed bottle → m-nitrotriphenylmethane. Y: 76%. F. e. s. C. N. Wolf and R. L. Shriner, J. Org. Chem. *15*, 367 (1950).

Aromatization ○
9(H)-Pyrid[3.4-b]indoles

780.

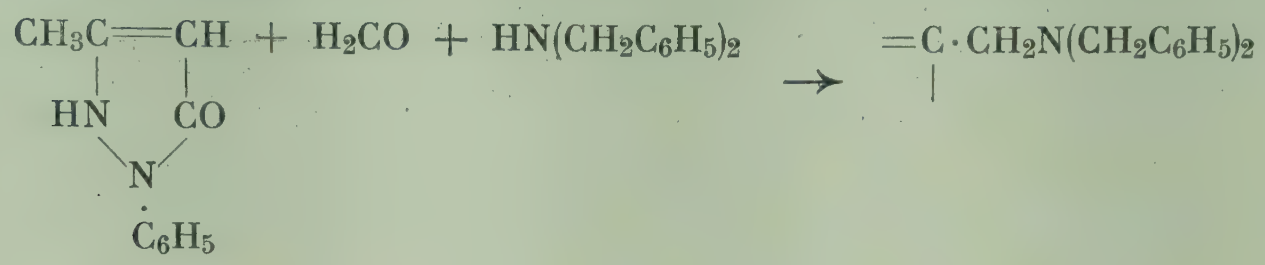


Alc. phenylacetaldehyde added to a soln. of tryptophan in *N* H_2SO_4, refluxed 4.5 hrs., more alcohol added, heated another 4 hrs., the crude tetrahydronoryobyrinecarboxylic acid so obtained dissolved in hot water, the boiling soln. treated with 10%-aq.-$K_2Cr_2O_7$ and acetic acid, then boiled 2 min. more → noryobyrine. Y: 56%. J. Keufer, Bl. *1950*, 109.

Ammonium chloride *NH_4Cl*

Aminomethylation
Mannich reaction $H \rightarrow CH_2NR_2$

781.

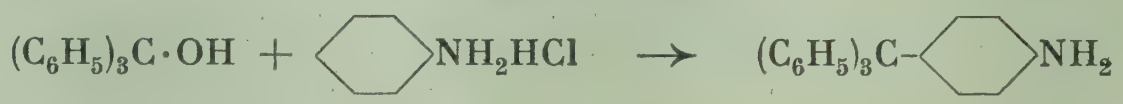


Antipyrine, dibenzylamine, formalin, and a little NH_4Cl in 95%-ethanol refluxed 2 hrs. → 4-(dibenzylaminomethyl)antipyrine. Y: 89%. F. e., reaction conditions, and mechanism s. S. V. Lieberman and E. C. Wagner, J. Org. Chem. *14*, 1001 (1949).

Hydrochlorides ←

Tetraarylmethanes from triarylcarbinols $C{\cdot}OH \rightarrow C{\cdot}R$

782.



Technical grade triphenylcarbinol, dry aniline hydrochloride, and glacial acetic acid refluxed 3 hrs. → p-aminotetraphenylmethane. Y: 70 to 74%. B. Witten and E. E. Reid, Org. Synth. *30*, 5 (1950).

C-Alkylation of ar. amines ←

s. *1*, 592; s. a. B. M. Dubinin and N. E. Kozhevnikova, Ж. *21*, 662 (1951); C. A. *45*, 9500c

Hydrofluoric acid *HF*

One-step indanone ring synthesis ○

s. *6*, 819

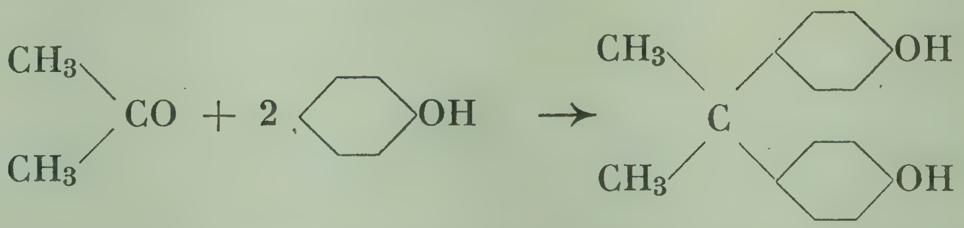
Hydrochloric acid *HCl*

Methylene bridging with formaldehyde $2\,RH \rightarrow R{\cdot}CH_2{\cdot}R$

s. *3*, 163; s. a. L. J. Smith and W. J. Dale, J. Org. Chem. *15*, 832 (1950)

1,1-Disubst. alkanes from ketones $CO \rightarrow CR_2$

783.



A mixture of acetone, phenol, and concd. HCl saturated with dry HCl-gas once a day during a week → 2,2-di-(p-hydroxyphenyl)propane. Y: 90%. P. W. Vittum and G. H. Brown, Am. Soc. *71*, 2287 (1949).

Chloromethylation H → CH_2Cl

s. *1,* 593-5, 597; *3,* 653; bis-chloromethylation s. J. H. Wood, M. A. Perry, and C. C. Tung, Am. Soc. *72,* 2989 (1950)

N-Cyanomethylation NH → NCH_2CN

s. *3,* 656; modified procedure s. R. A. Turner and C. Djerassi, Am. Soc. *72,* 3081 (1950)

Einhorn amidomethylation H → CH_2NHCOR
Condensation with hydroxymethylamides

s. 3, 657; 5, 562; s. a. A. M. Downes and F. Lions, Am. Soc. *72,* 3053 (1950); R. D. Haworth, R. MacGillivray, and D. H. Peacock, Soc. *1950,* 1493

α,β-Ethyleneketones CH : CHCO

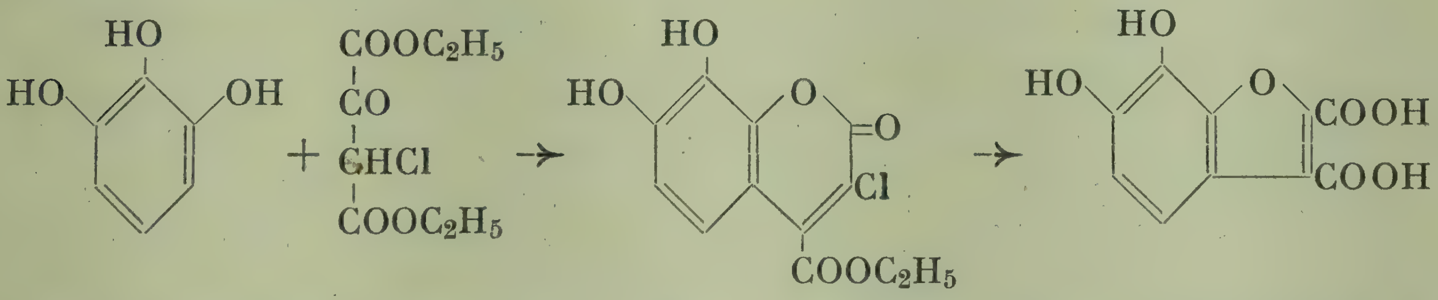
s. *5,* 563; s. a. J. Schläger and W. Leeb, M. *81,* 714 (1950)

Benzopyrylium salts ○

s. *1,* 603; s. a. D. A. Collins et al., Soc. *1950,* 1876; R. R. Otter and R. L. Shriner, Am. Soc. *73,* 887 (1951)

Benzofurans via 3-halogenocoumarins
Perkin transformation

784.

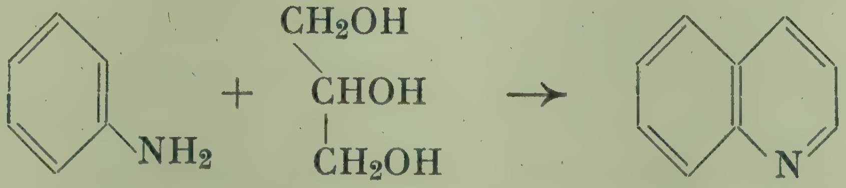


6 gm. pyrogallol and 10.6 gm. ethyl β-chloro-β-carbethoxypyruvate in alcohol with excess of HCl allowed to stand for 3 days → 11.5 gm. ethyl 3-chloro-7,8-dihydroxycoumarin-4-carboxylate, 3 gm. of which heated on a steam bath with oxygen-free aq. 10%-KOH in a N_2-atmosphere for 45 min. → 2 gm. 6,7-dihydroxycoumarone-2,3-dicarboxylic acid. F. e. s. G. W. Holton, G. Parker, and A. Robertson, Soc. *1949,* 2049; transformation s. a. V. J. Dalvi and S. Sethna, J. Indian Chem. Soc. *26,* 359, 467 (1949).

Ferrous sulfate/nitrobenzene ←

Skraup quinoline synthesis

85.



Moderation of violence and increase in yield are obtained by adding the amine followed by glycerol to the concd. H_2SO_4 with cooling at

70-90°. This premix is then added portionwise to the nitro compound and $FeSO_4$.—E.: A mixture of aniline, glycerol, and concd. H_2SO_4 added portionwise to nitrobenzene and $FeSO_4 \cdot 7H_2O$ preheated to 100 to 120°, at such a rate that the exothermic reaction proceeds at 160 to 170°, and refluxed 4 hrs. → quinoline. Y: ca. 100%. F. e. s. R. H. F. Manske, A. E. Ledingham, and W. R. Ashford, Can. J. Research *27F*, 359 (1949).

Via intermediates *v.i.*

Nitriles from alcohols via chlorides OH → CN

s. *6*, 812

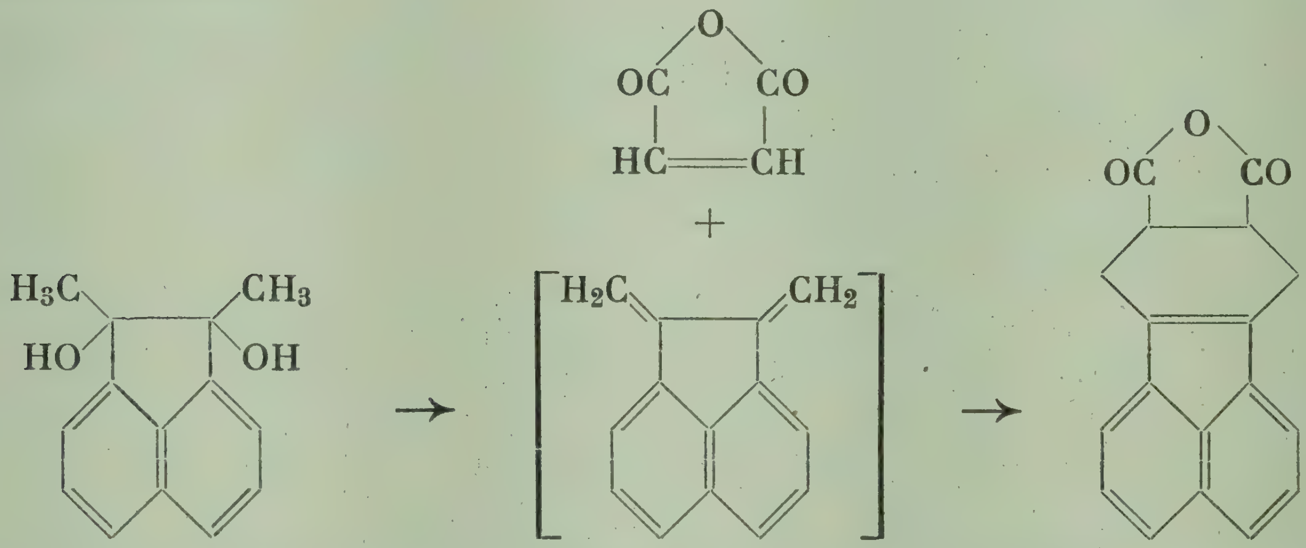
Gränacher synthesis via rhodanine CHO → CH_2CN

Nitriles from aldehydes

s. *3*, 662; s. a. F. E. King and M. F. Grundon, Soc. *1950*, 3547; J. C. Sheehan and C. A. Robinson, Am. Soc. *73*, 1207 (1951)

Diene synthesis ○

786.



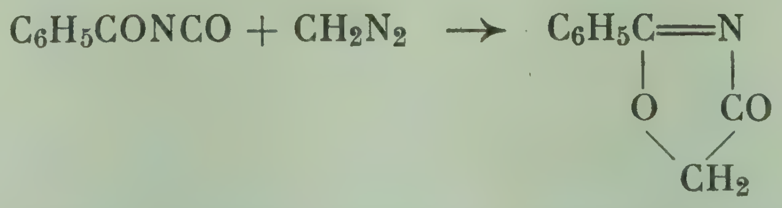
trans-7,8-Dimethylacenaphthene-7,8-diol, maleic anhydride, and acetic anhydride refluxed 15 min. → 10,11,12,13-tetrahydro-11,12-fluoranthenedicarboxylic anhydride. Y: 70%.—Less reactive dienophiles give only polymeric products. F. e. s. N. Campbell and R. S. Gow, Soc. *1949*, 1555, 1513 (1949).

Nitrogen ↑ CC ⇅ N

Without additional reagents *w.a.r.*

Oxazolones from acylisocyanates and diazomethane ○

787.



$$C_6H_5CONCO + CH_2N_2 \rightarrow \begin{array}{c} C_6H_5C{=}N \\ |\quad\;\; | \\ O\quad CO \\ \diagdown\;\diagup \\ CH_2 \end{array}$$

Ethereal diazomethane added slowly to ethereal benzoyl isocyanate, then allowed to stand at room temp. for 1 hr. and at 0-5° overnight

→ 2-phenyl-4-oxazolone. Y: 68%. J. C. Sheehan and P. T. Izzo, Am. Soc. *71*, 4059 (1949).

Ring enlargement of cyclic ketones ←
s. *5*, 571; s. a. Bl. *1949*, 392

Sodium hydroxide *NaOH*

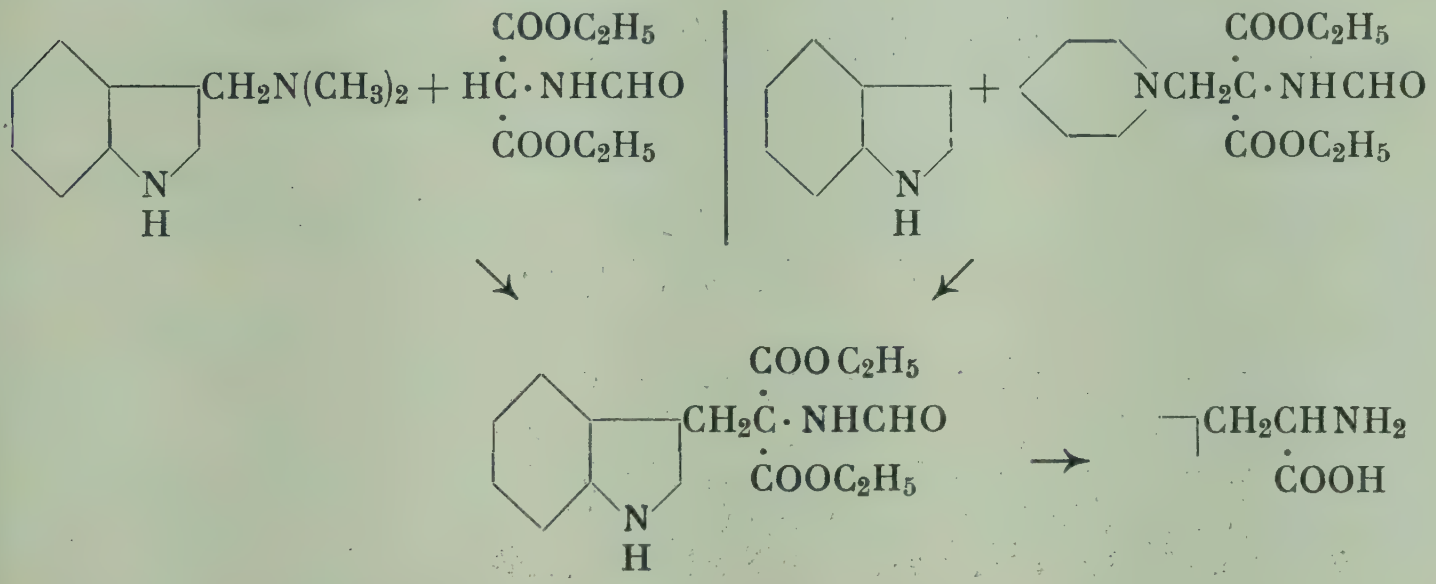
N-Carboxymethylation ←

88. $H_2NCH_2COOH + 2\ H_2CO + 2\ NaCN \longrightarrow N(CH_2COOH)_3$

A soln. of glycine in aq. NaOH treated alternately with a soln. of NaCN in NaOH and 37%-formaldehyde at 80° with vigorous stirring over a period of 8 hrs., allowed to stand overnight, then heated to 100° on a water bath, and stirred for 2 hrs. → triglycine. Y: 93%. A. E. Martell and F. C. Bersworth, J. Org. Chem. *15*, 46, 255 (1950).

Syntheses with tert. amines ←

89.



3-(Diethylaminomethyl)indole and diethyl formamidomalonate added to boiling dry toluene containing powdered NaOH, and refluxed 0.5–1 hr. in a vigorous N_2-stream → Y: 98%

A mixture of indole, diethyl (1-piperidylmethyl)formamidomalonate (prepn. s. 732), and powdered NaOH refluxed 5 hrs. in anhydrous xylene in an N_2-stream → Y: 76%

diethyl (skatyl)formamidomalonate

and aq. NaOH heated 6 hrs. at an oil-bath temp. of 120–130°, acetic acid added, and heating continued at 130° for 1–2 hrs. → DL-tryptophan (Y: 96%).

H. Hellmann et al., Z. physiol. Chem. *284*, 163, 175 (1949).

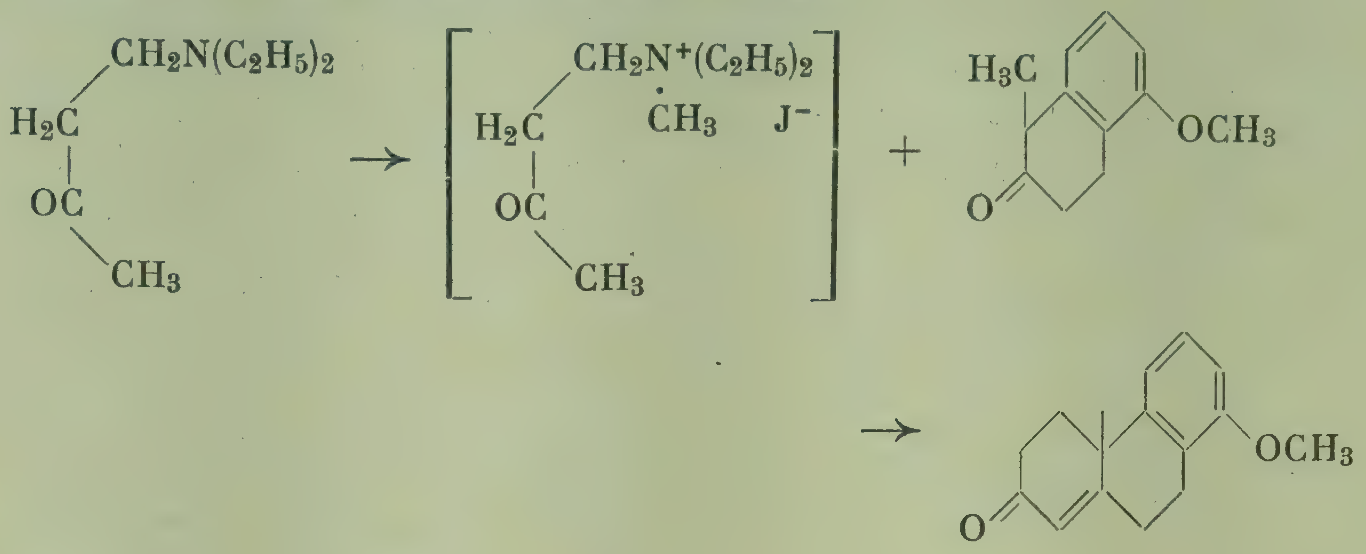
Sodium/alcohol *NaOR*

s. *3*, 665; *4*, 754; s. a. N. J. Leonard and E. H. Burk, Jr., Am. Soc. *72*, 2543 (1950)

Potassium/alcohol *KOR*

Synthesis of isocyclics with tert. amines ○

790.

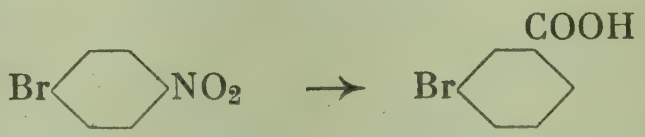


Methyl iodide added with swirling and ice-cooling during 0,5 hr. to 4-diethylamino-2-butanone, when all has solidified kept in ice for 0.5 hr., then under the tap for 45 min., a soln. of 5-methoxy-1-methyl-2-tetralone in dry, thiophene-free benzene added, the air expelled by dry N_2, a soln. of K in dry ethanol added with ice-cooling during 5 min., swirling continued until the methiodide has all dissolved after ca. 30 min., kept in ice for another hr., and boiled gently for 25 min. → 7-keto-1-methoxy-13-methyl-5,6,7,9,10,13-hexahydrophenanthrene. Y: 71%.— This procedure is suitable for large scale preparations. J. W. Cornforth and R. Robinson, Soc. *1949*, 1855.

Potassium cyanide *KCN*

von Richter reaction ←
Position shift of substituents of isocyclics
Carboxylic acids from nitro compounds

791.



p-Nitrobenzene heated at 145-155° with KCN in 48%-alcohol in a sealed tube for 1 hr. → m-bromobenzoic acid. Y: 22%. F. e. s. J. F. Bunnett, J. F. Cormack, and F. C. McKay, J. Org. Chem. *15*, 481 (1950).

Sodium nitrite *$NaNO_2$*

Carboxylic acids from aminosulfonic acids
Replacement of amino groups
by cyano groups
s. *4*, 757; s. a. Bl. *1950*, 757

Union of aryl nuclei Ar + Ar′ → Ar·Ar′

s. *1*, 608; arylquinols s. G. B. Marini-Bettòlo, O. A. Polla, and J. H. Abril, G. *80*, 76 (1950)

Cuprous cyanide *CuCN*

Replacement of amino by cyano groups $NH_2 \rightarrow CN$

s. *3*, 666; s. a. C. A. Grob and H. U. Schmid, Helv. *33*, 1955 (1950); in strongly acid soln. s. H. Bretschneider and H. Rager, M. *81*, 970 (1950)

Cupric sulfate *$CuSO_4$*

Diaryls from arylamines $2\,RNH_2 \rightarrow R \cdot R$
Dimerization

s. *2*, 701; s. a. E. R. Atkinson, D. M. Murphy, and J. E. Lufkin, Org. Synth. *31*, 96 (1951)

Cupric chloride *$CuCl_2$*

Diazo coupling ←

92. $$C_6H_5N_2Cl + CH_2{=}CHCN \rightarrow C_6H_5CH_2CHClCN$$

A soln. of $CuCl_2$ in a small amount of water added to acrylonitrile, Na-acetate, benzenediazonium chloride soln., and acetone, and worked up after 1.5 hrs. at 10-11° → α-chloro-β-phenylpropionitrile. Y: 81%. F. e. s. W. H. Brunner et al., M. *79*, 187 (1948); *82*, 100 (1951).

1,4-Addition

s. *4*, 760; s. a. Am. Soc. *72*, 3960 (1950); Org. Synth. *31*, 80 (1951)

Hexamethylenetetramine/boric acid *$C_6H_{12}N_4/HBO_2$*

Introduction of the aldehyde group into ar. nuclei $H \rightarrow CHO$
Hydroxy aldehydes from phenols

o-Hydroxyaldehydes s. *1*, 621; *3*, 667; p-hydroxyaldehydes s. C. F. H. Allen and G. W. Leubner, Org. Synth. *31*, 92 (1951)

Phosphorus oxychloride *$POCl_3$*

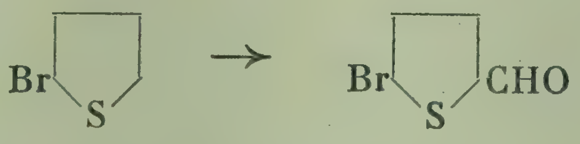
Aldehyde synthesis with methylformanilide $H \rightarrow CHO$

Heterocyclic aldehydes

s. *3*, 668; formylthiophenes s. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, Soc. *1950*, 2130; A. W. Weston and R. J. Michaels, Jr., Org. Synth. *31*, 108 (1951); carbazole aldehydes s. Am. Soc. *73*, 98 (1951)

Phosphorus oxybromide *$POBr_3$*

93.



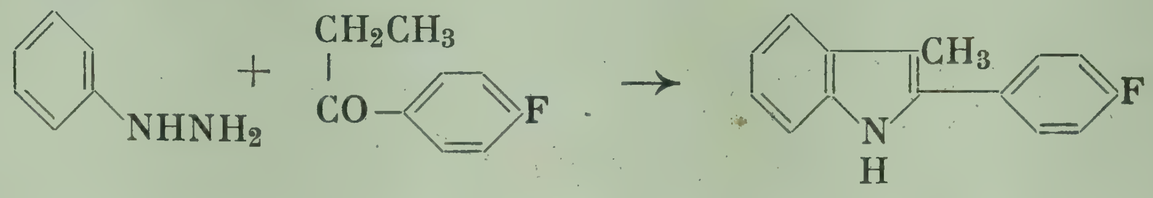
2-Bromothiophene added dropwise to a soln. of $POBr_3$ and N-methylformanilide in chlorobenzene at 50°, and stirred 18 hrs. at room temp.

→ 5-bromo-2-thiophenecarboxaldehyde. Y: 70%.—This reaction proceeds well at room temp.—Halogen interchange can be avoided by using $POBr_3$ in place of $POCl_3$. F. e. with $POCl_3$ s. A. W. Weston and R. J. Michaels, Jr., Am. Soc. *72*, 1422 (1950).

Hydrochloric acid *HCl*

Fischer indole ring synthesis ○

794.



A mixture of p-fluoropropiophenone and phenylhydrazine heated to 200° with evaporation of the water formed, allowed to cool, acetic acid saturated with HCl gas added, and cautiously refluxed several min. → 2-(4′-fluorophenyl)skatole. Y: ca. 75%. F. e. s. Ng. Ph. Buu-Hoï, Ng. Hoán, and P. Jacquignon, R. *68*, 781 (1949); Soc. *1949*, 2882. When the hydrazines used are decomposed at elevated temp., the hydrazones must be isolated before the cyclization. R. *68*, 441 (1949).

Halogen ↑ CC ⇅ Hal

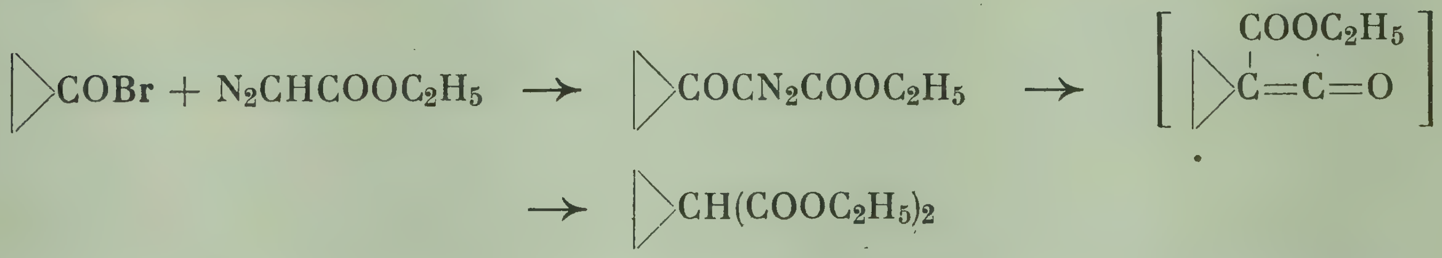
Without additional reagents *w.a.r.*

Condensation with elimination of hydrogen halides RHal + HR′ → R·R′

s. *5*, 577; s. a. E. Ziegler, M. *79*, 142 (1948); H. Hart and J. H. Simons, Am. Soc. *71*, 345 (1949)

Malonic acid esters from carboxylic acid bromides via diazo compounds $COBr \rightarrow CH(COOR)_2$

795.

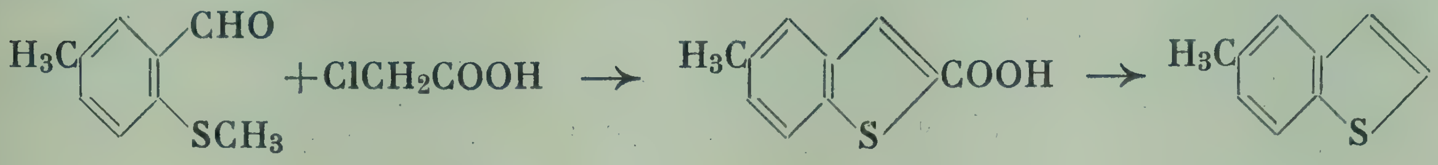


Cyclopropanecarboxylyl bromide added with stirring to an ethereal soln. of ethyl diazoacetate, cooled for a few moments until the N_2-evolution subsides somewhat, allowed to stand 1 day at room temp., then refluxed gently for 2 days → ethyl cyclopropanecarboxylyldiazoacetate (Y: 72%) refluxed 3-4 hrs. with Ag_2O and toluene under CO_2 until the N_2-evolution ceases, the toluene removed, and the residue distilled in vacuo into cooled ethanol → ethyl cyclopropylmalonate (Y: 43%). L. I. Smith and S. McKenzie, Jr., J. Org. Chem. *15*, 74 (1950).

Thianaphthenes Decarboxylation

○

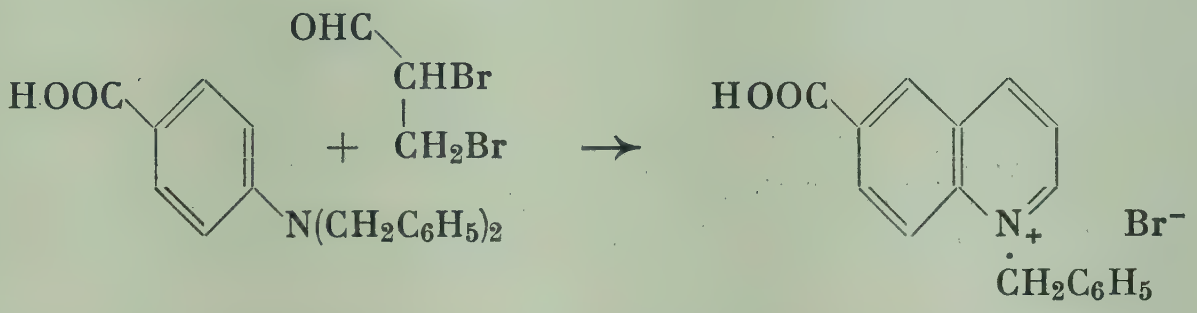
796.



2-Methylmercapto-5-methylbenzaldehyde and chloroacetic acid heated 10 hrs. in a boiling water bath → 5-methylthianaphthene-2-carboxylic acid (Y: 88%) mixed intimately with $Ca(OH)_2$, and distilled → 5-methylthianaphthene (Y: 90%). F. e. with ketones s. F. Krollpfeiffer, K. L. Schneider, and A. Wissner, A. *566*, 139 (1950).

Synthesis of quinolinium salts

797.



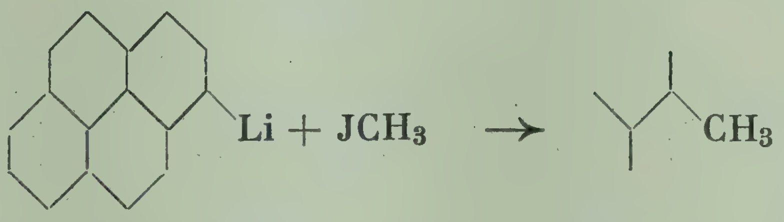
N,N-Dibenzyl-p-aminobenzoic acid and acrolein dibromide in dioxane boiled 75 min. in an oil bath → 1-benzyl-6-carboxyquinolinium bromide. Y: 75%. F. e. s. F. Weygand and W. Rupp, Chem. B. *83*, 455 (1950).

Lithium *Li*

Synthesis of hydrocarbons from halides

RHal → R·R

798.



Crystalline 3-pyrenyl-Li allowed to react with methyl iodide in ether, and worked up after 15 min. → 3-methylpyrene. Y: 83%. F. e. s. A. Berg, Acta Chem. Scand. *3*, 655 (1949); s. a. V. Boekelheide and C. E. Larrabee, Am. Soc. *72*, 1245 (1950); G. Wittig et al., A. *566*, 101 (1950); B. *83*, 359 (1950).

o-Alkylation and o-arylation of N-heterocyclics

isoquinolines s. *4*, 768; pyridines s. E. Doering and V. Z. Pasternak, Am. Soc. *72*, 143 (1950); quinolines s. J. P. Philipps, R. L. Elbinger, and L. L. Merritt, Jr., Am. Soc. *71*, 3986 (1949)

Sodium *Na*

Synthesis of hydrocarbons from halides $\mathrm{RHal + HR' \rightarrow R{\cdot}R'}$

s. *2*, 710b; s. a. D. Bryce-Smith and E. E. Turner, Soc. *1950*, 1975

Wurtz-Fittig synthesis $\mathrm{C{\cdot}Hal + Hal{\cdot}C \rightarrow C{\cdot}C}$

s. *1*, 633; *2*, 710/a; *3*, 669; ring closure s. A. C. Cope and S. W. Fenton, Am. Soc. *73*, 1668 (1951)

Synthesis of hydrocarbons from ethers ←

s. *5*, 581; optically active compounds s. Am. Soc. *72*, 849 (1950)

Sodium hydroxide *NaOH*

Introduction of the aldehyde group into ar. nuclei according to Reimer-Tiemann $\mathrm{H \rightarrow CHO}$

s. *2*, 714; *3*, 670; s. a. G. S. Kolesnikov, V. V. Korshak, and J. P. Krakovnaya, Ж. *21*, 397 (1951); C. A. *45*, 7553c

Sodium/alcohol *NaOR*

Alkylation of β-ketocarboxylic acid esters $\mathrm{{\cdot}HC(COR)COOR' \rightarrow {\cdot}R''C(COR)COOR'}$

s. *1*, 637; *2*, 717/8, 827; s. a. G. Tschudi and H. Schinz, Helv. *33*, 1865 (1950)

Alkylation of acylaminomalonic esters
α-Aminocarboxylic acids from halides $\mathrm{Hal \rightarrow CH(NH_2)COOH}$
Synthesis with addition of 2 C-atoms

s. *3*, 674; s. a. J. H. Burckhalter and V. C. Stephens, Am. Soc. *73*, 56 (1951)

Alkylation of α-cyanocarboxylic acid esters $\mathrm{{\cdot}HC(CN)COOR \rightarrow {\cdot}R'C(CN)COOR}$

s. *6*, 802

Sodium-tert-amylate

Alkylation of ketones $\mathrm{COCH \rightarrow COCR}$

s. *3*, 671; s. a. Bl. *1950*, 533, 537

Sodium/liq. ammonia *Na/NH_3*

Acetylenehalides from dihalides $\mathrm{Hal \rightarrow C{\vdots}CR}$

s. *5*, 588; from iodochlorides s. W. R. Taylor and F. M. Strong, Am. Soc. *72*, 4263 (1950)

Partial alkylation of diacetylene derivatives

799. $CH{\equiv}C{\cdot}[CH_2]_4{\cdot}C{\equiv}CH + JCH_2CH_2CH_3 \longrightarrow CH{\equiv}C{\cdot}[CH_2]_4{\cdot}C{\equiv}C{\cdot}CH_2CH_2CH_3$

Octa-1,7-diyne in dry ether added during 10 min. with stirring and alcohol-CO_2-cooling to a suspension of 1.1 moles of $NaNH_2$ in liq. NH_3 (prepared from Na with $Fe(NO_3)_3$ catalyst according to Vaughan, Vogt, and Nieuwland, Am. Soc. *56,* 2120 (1934)), stirred 2 hrs., propyl iodide in ether gradually added, and stirring continued for another 6 hrs. at ca. —40° → undeca-1,7-diyne. Y: 86%; conversion 49%.— Propyl bromide gives a much lower yield. F. e. s. R. A. Raphael and F. Sondheimer, Soc. *1950,* 115, 120.

Sodium amide *$NaNH_2$*

Aminoalkylation of ketones

COCH → COCR

s. *3,* 679; s. a. W. G. Stoll, C. Frey, and C. J. Morel, Helv. *33,* 1208 (1950); cf. N. Sperber, R. Fricano, and D. Papa, Am. Soc. *72,* 3068 (1950)

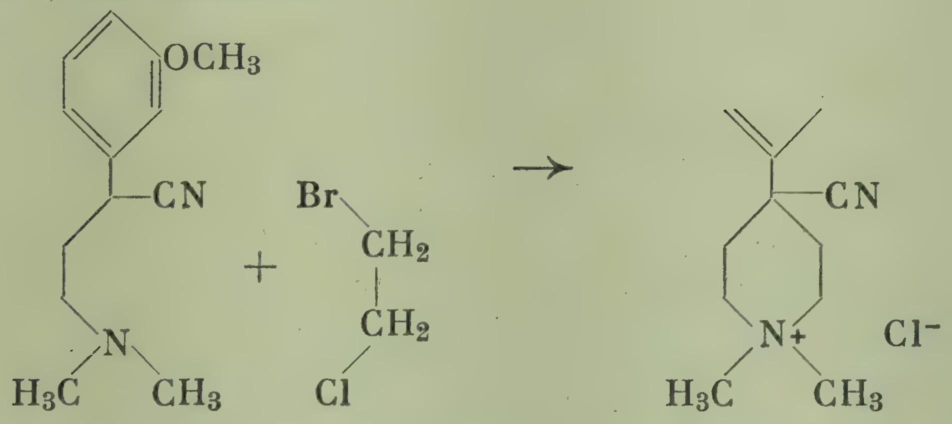
Alkylation of nitriles

CHCN → CRCN

s. *1,* 656; *3,* 680; *4,* 774; s. a. R. Paul and S. Tschelitcheff, Bl. *1949,* 470

Piperidinium ring synthesis ○

800.



Dimethylaminoethyl-m-methoxybenzyl cyanide added dropwise at 20° to powdered $NaNH_2$ in toluene with stirring and water-cooling, stirring continued for 5 hrs. at the same temp., cooled to 10°, ethylene chlorobromide added at 8-10°, and worked up after ¼ hr. → 1,1-dimethyl-4-m-methoxyphenyl-4-cyanopiperidinium chloride. Y: 70%. F. e. s. H. Kägi and K. Miescher, Helv. *32,* 2489 (1949).

Potassium amide *KNH_2*

Ketones from carboxylic acid chlorides

COCl → COR

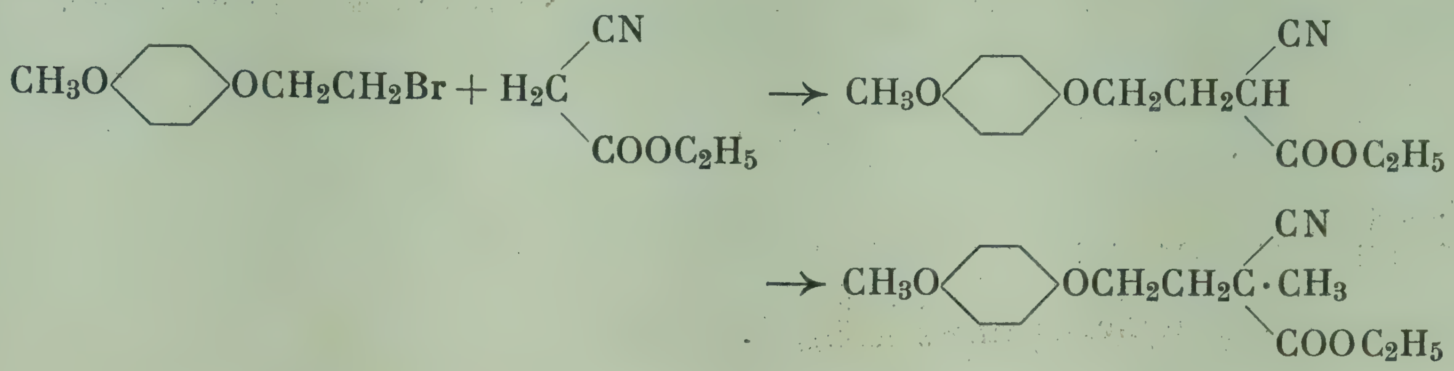
801. $(C_6H_5)_3C{\cdot}COCl + H_2C(C_6H_5)_2 \longrightarrow (C_6H_5)_3C{\cdot}CO{\cdot}CH(C_6H_5)_2$

A soln. of triphenylacetyl chloride in dry benzene added rapidly to a suspension of K-diphenylmethide (prepared from diphenylmethane and KNH_2) in ether cooled in a Dry Ice-acetone bath, then refluxed 24 hrs. → pentaphenylacetone. Y: 70-87%. F. e. s. S. W. Kantor and C. R. Hauser, Am. Soc. *72,* 3290 (1950).

Potassium carbonate *K_2CO_3*

Alkylation of α-cyanocarboxylic acid esters $\cdot HC(CN)COOR \rightarrow \cdot R'C(CN)COOR$

802.

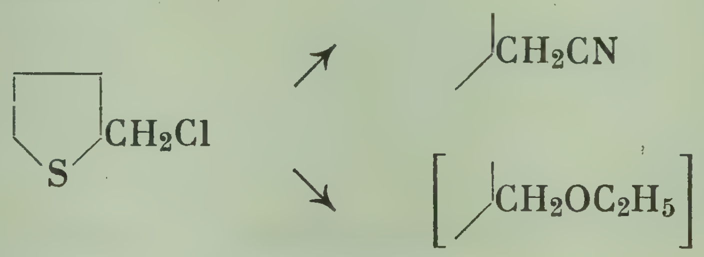


A mixture of 1-bromo-2-(p-methoxyphenoxy)ethane, anhydrous K-carbonate, and ethyl cyanoacetate refluxed 22 hrs. at 130°/120 mm. → ethyl-α-cyano-γ-(p-methoxyphenoxy)butyrate (Y: 81%) added to a soln. of Na in abs. ethanol, stirred and treated at reflux temp. with methyl iodide over a period of 0.5 hr., and refluxing continued for 5 hrs. → ethyl α-cyano-α-methyl-γ-(p-methoxyphenoxy)butyrate (startg. m. f. 12) (Y: 91%). N. J. Leonard and W. C. Wildman, Am. Soc. *71*, 3089 (1949).

Potassium cyanide *KCN*

Nitriles from chlorides Cl → CN

803.



2-(Chloromethyl)thiophene and KCN in *acetone* refluxed 6 hrs. → 2-thienylacetonitrile. Y: 80%.—In alcohol-water 30% of α-(ethoxymethyl)thiophene are formed as by-product. P. Cagniant, Bl. *1949*, 847 (1949).

Triethylamine *$(C_2H_5)_3N$*

Ketenedimers from carboxylic acid chlorides ←

s. *4*, 779; cf. C. M. Hill et al., Am. Soc. *73*, 1660 (1951)

Copper *Cu*

Dimerization

Diaryls from arylhalides 2 RHal → R·R

s. *1*, 660-2; s. a. H. Brockmann, R. Neeff, and E. Mühlmann, B. *83*, 467 (1950)

Ethylene derivatives from 1,1-dihalides $2\ RCl_2 \rightarrow R:R$

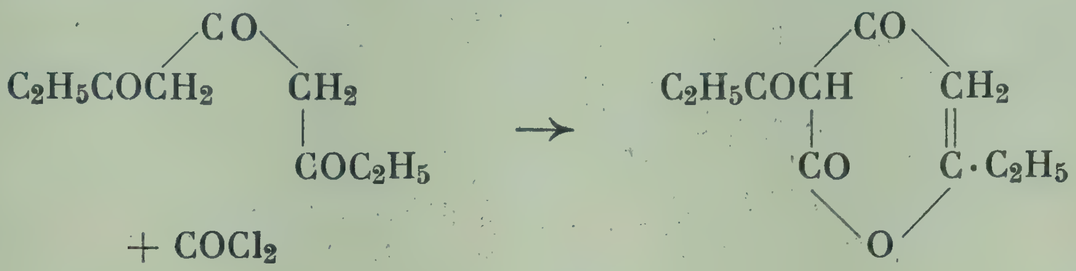
s. *5*, 594; s. a. R. E. Buckles and G. M. Matlack, Org. Synth. *31*, 104 (1951)

Introduction of carboxylic groups into ar. rings H → COOH
s. *6,* 763

Cupric acetate *$(CH_3COO)_2Cu$*

Pyran ring synthesis ○

804.



A cold satd. soln. of Na-acetate and Cu-acetate added to an alc. soln. of dipropionylacetone, 5.7 gm. of the dry Cu-salt of dipropionylacetone so obtained (Y: almost 100%), suspended in dry benzene, a soln. of 2.6 gm. $COCl_2$ in benzene added with cooling, kept at 0° for 5 hrs. with occasional shaking, then allowed to stand at room temp. for 5 days → 2.5 gm. dehydropropionylacetic acid. F. e. s. M. M. Mahala and S. S. Deshapande, J. Indian Chem. Soc. *26,* 429 (1949).

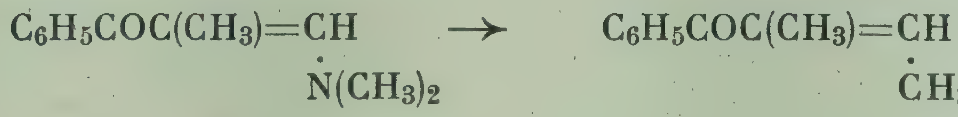
Cuprous cyanide *CuCN*

Acylcyanides from carboxylic acid chlorides COCl → COCN
s. *6,* 898

Magnesium *Mg*

Hydrocarbons from tert. amines R·N → R·R′

805.

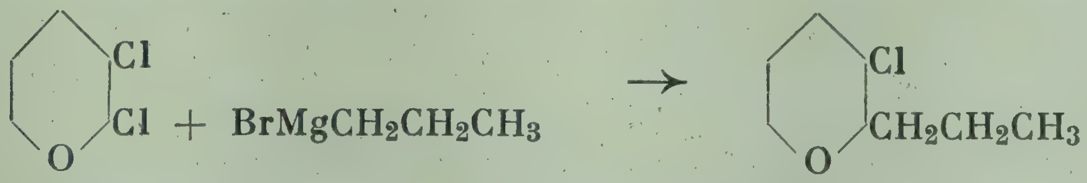


$$C_6H_5COC(CH_3){=}\underset{N(CH_3)_2}{\underset{\cdot}{CH}} \rightarrow C_6H_5COC(CH_3){=}\underset{CH_3}{\underset{\cdot}{CH}}$$

α-(Dimethylaminomethylene)propiophenone in dry ether added dropwise at 0° to a stirred ethereal soln. of methyl-MgI, and stirring continued for 40 min. → α-methyl-α-butenophenone. Y: 71%. L. I. Smith and V. A. Engelhardt, Am. Soc. *71,* 2671 (1949).

Selective replacement of chlorine by alkyl RHal + HalR′ → R·R′

806.



2,3-Dichlorotetrahydropyran in ether added over a period of 4.5 hrs. with stirring and occasional cooling to an ethereal soln. of *n*-propyl-MgBr at such a rate that gentle refluxing is maintained → 3-chloro-2-*n*-propyltetrahydropyran. Y: 73%. M. Jacobson, Am. Soc. *72,* 1489 (1950); s. a. R. Paul and S. Tchelitcheff, Bl. *1948,* 1199; L. Crombie and S. H. Harper, Soc. *1950,* 1707, 1714.

Dimerization of halides

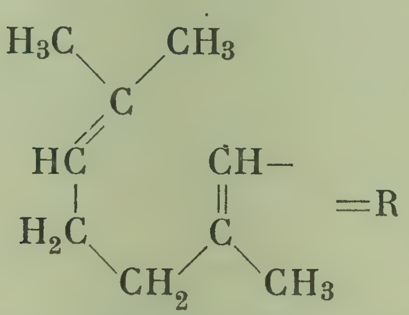
2 RHal → R·R

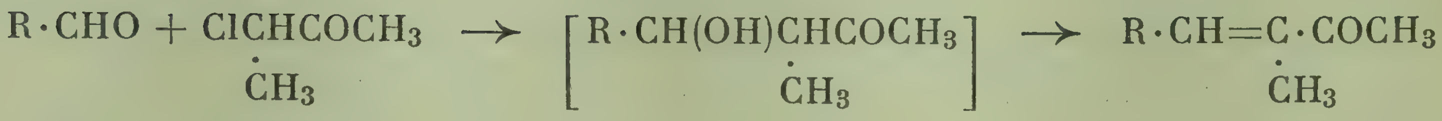
of chlorides s. *1*, 668; *4*, 780; of bromides s. E. H. Farmer and C. G. Moore, Soc. *1951*, 131

Ethylene derivatives from aldehydes

CHO → CH:CH

807.





$$R\cdot CHO + \underset{CH_3}{ClCHCOCH_3} \rightarrow \left[R\cdot CH(OH)\underset{CH_3}{CHCOCH_3}\right] \rightarrow R\cdot CH{=}\underset{CH_3}{C}\cdot COCH_3$$

α,β-Ethyleneketones. A vigorously reacting mixture of Mg, ethyl bromide, and dry ether added to a mixture of Mg (etched by a trace of iodine) and 3-chlorobutan-2-one, free of HCl, then a mixture of citral, more 3-chlorobutan-2-one, and dry ether added under N_2 and gentle refluxing, stirring and refluxing continued until the visible reaction has stopped, thereafter an additional hr., and the product distilled quickly, whereby water is split off → pseudoisomethylionone. Y: up to 48%.—By using chloroketone in place of bromoketone, the yield could be considerably improved. M. G. J. Beets, R. *69*, 307 (1950).

Aldehydes from halides

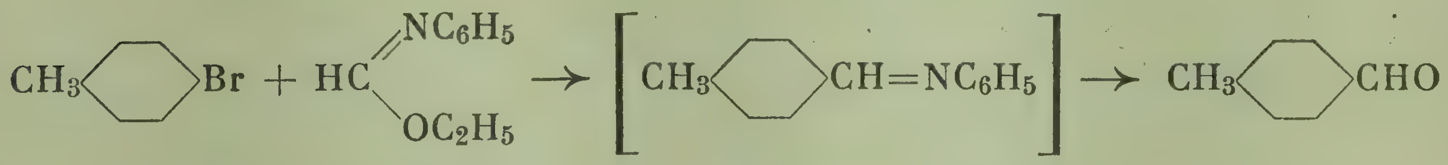
Hal → CHO

with orthoformic acid esters

s. *1*, 683; s. a. Y. Hirshberg, E. and F. Bergmann, Am. Soc. *72*, 5120 (1950)

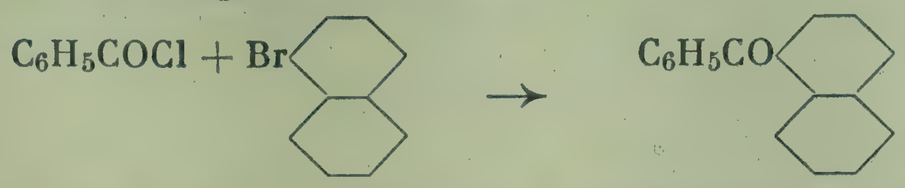
with N-phenylformimidate

808.



N-Phenylformimidate (prepn. s. 234) added dropwise at room temp. to p-tolyl-Mg-bromide (prepared from p-bromotoluene and Mg in ether in the presence of ethyl bromide and a crystal of iodine), refluxed 30 min., decomposed with ice-HCl, and refluxed another 30 min. to hydrolyze the anil → p-tolualdehyde. Y: 82.2% as bisulfite compound. F. e. s. L. I. Smith and J. Nichols, J. Org. Chem. *6*, 489 (1941).

Ketones from carboxylic acid chlorides COCl → COR
Steric hindrance in Grignard reactions

809. 

A certain amount of steric hindrance is necessary to obtain ketones from carboxylic acid chlorides and Grignard compounds. Certain mono-ortho subst. Grignard compounds give ketones with equimolecular proportions and reverse order of addition.—E: An ethereal soln. of 1-naphthyl-MgBr added slowly with stirring and ice-cooling to an ethereal soln. of benzoyl chloride, and heated for 5 hrs. → phenyl 1-naphthyl ketone. Y: 69%. F. e. s. I. I. Lapkin and A. V. Lyubimova, Ж. *19*, 707 (1949); C. A. *44*, 1058a.

Ketocarboxylic acids from dicarboxylic acid anhydrides ←

810. This method is superior to the Friedel-Crafts' in those cases where nitrobenzene or tetrachloroethane must be used as a solvent, and may also serve for the determination of the orientation of the acids produced by the Friedel-Crafts method. E. s. J. A. McRae, R. A. B. Bannard, and R. B. Ross, Can. J. Research *28B*, 73 (1950).

1-Subst. 1,2-dihydroisoquinolines ←
s. *5*, 600; s. a. G. Wittig et al., A. *572*, 15 (1951)

Magnesium/cuprous chloride *Mg/CuCl*

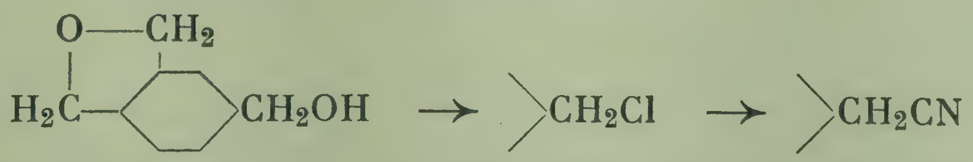
Highly branched ketones from carboxylic acid chlorides COCl → COR

811. $(CH_3)_3C \cdot MgCl + ClCOC(CH_3)_3 \rightarrow (CH_3)_3C \cdot CO \cdot C(CH_3)_3$

A filtered 3 *M* soln. of *tert*-butyl-MgCl added at reflux temp. over a 1 hr. period to a soln. of trimethylacetyl chloride and CuCl in anhydrous ether, most of the solvent distilled off, then heated at 100° for 3 days → hexamethylacetone. Y: 71.6%.—Reactions in glass without CuCl gave only a yield of 1-2%. Yields with straight chain reactants are not as markedly improved as with highly branched ones. N. C. Cook and W. C. Percival, Am. Soc. *71*, 4141 (1949).

Mercuric cyanide *Hg(CN)₂*

Nitriles from alcohols via chlorides OH → CN
Synthesis with addition of 1 C-atom

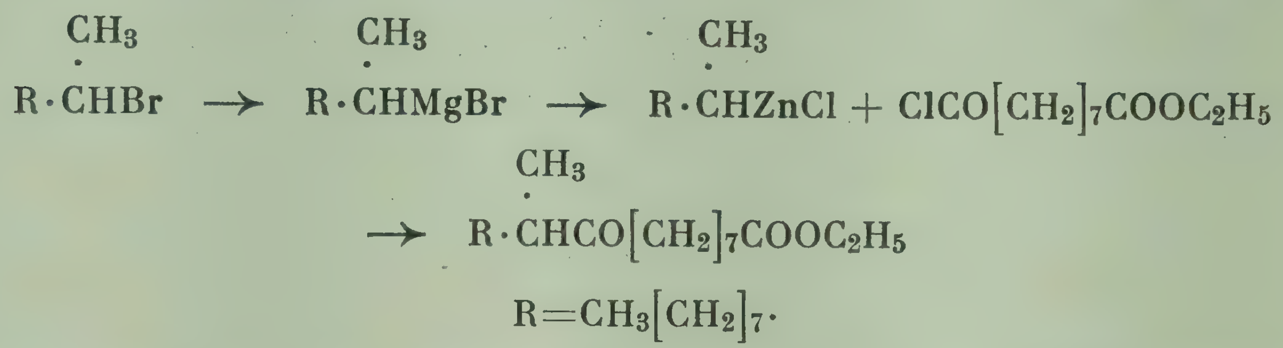
812. 

Piperonyl alcohol allowed to react with concd. HCl and sufficient $CaCl_2$ to saturate the aq. layer → 3,4-methylenedioxybenzyl chloride in benzene stirred and refluxed 6 hrs. with aq. NaCN and some $Hg(CN)_2$ → 3,4-methylenedioxybenzyl cyanide (startg. m. f. 76). Y: 85%. W. Reeve and W. M. Eareckson, 3rd, Am. Soc. *72*, 3299 (1950); replacement of hydroxyl by chlorine s. a. J. F. Norris and J. T. Blake, Am. Soc. *50*, 1808 (1928); A. W. Billitzer, Australian Chem. Inst. J. & Proc. *15*, 261 (1948).

Zinc chloride *$ZnCl_2$*

Ketones from carboxylic acid chlorides COCl → COR

813.



$$R\cdot\overset{CH_3}{\dot{C}H}Br \rightarrow R\cdot\overset{CH_3}{\dot{C}H}MgBr \rightarrow R\cdot\overset{CH_3}{\dot{C}H}ZnCl + ClCO[CH_2]_7COOC_2H_5 \rightarrow R\cdot\overset{CH_3}{\dot{C}H}CO[CH_2]_7COOC_2H_5 \qquad R{=}CH_3[CH_2]_7\cdot$$

An ethereal soln. of 2-decyl-MgBr added to a soln. of freshly fused anhydrous $ZnCl_2$ in ether at such a rate that gentle reflux is maintained, part of the solvent distilled off during 1.5 hrs., a soln. of ω-carbethoxyoctanoyl chloride in anhydrous benzene added with stirring, and refluxed 3 hrs. → ethyl 9-keto-10-methylyloctadecanoate. Y: 93%, based on acid chloride consumed.—The organo-Cd-compounds, usually found advantageous for ketone formation, are not satisfactory when secondary types are used. G. A. Schmidt and D. A. Shirley, Am. Soc. *71*, 3804 (1949).

Cadmium chloride *$CdCl_2$*

s. *3*, 694; s. a. W. G. Dauben and H. Tilles, J. Org. Chem. *15*, 785 (1950); H. Heusser et al., Helv. *33*, 2229, 2237 (1950); modification for highly reactive carbonyl groups s. R. Pinson, Jr., and S. L. Friess, Am. Soc. *72*, 5333 (1950)

Aluminum chloride *$AlCl_3$*

Friedel-Crafts ketone synthesis RH → RCOR′

α,β-Ethyleneketones

814. $CH_3COCl + CH_2{=}CCl_2 \rightarrow CH_3COCH{=}CCl_2$

Finely powdered $AlCl_3$ slowly added with vigorous stirring to acetyl chloride cooled in a freezing mixture, then vinylidene chloride slowly dropped in at room temp. during 1.5 hrs., and stirred for a further 0.5 hr. → methyl 2,2-dichlorovinyl ketone (startg. m. f. 686). Y: 80%. I. M. Heilbron, E. R. H. Jones, and M. Julia, Soc. *1949*, 1430.

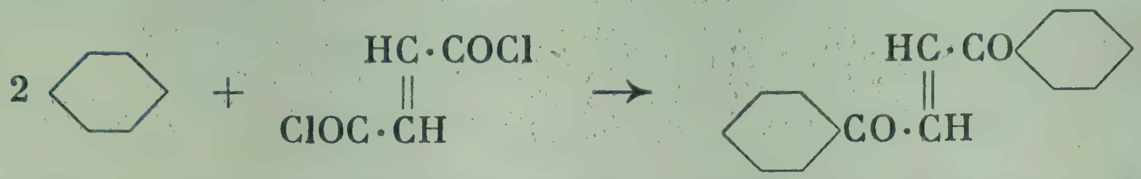
Perrier procedure

s. *2*, 748; *3*, 697; s. a. C. K. Bradsher and I. Swerlick, Am. Soc. *72*, 4189 (1950)

1,2-Diaroylethylenes

COCH : CHCO

815.

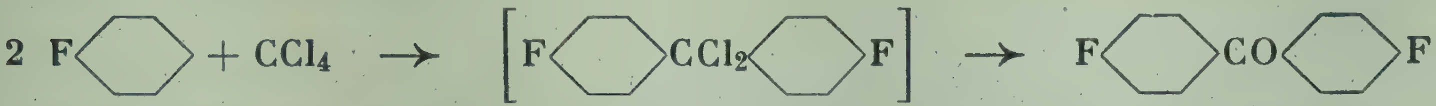


Fumaryl chloride added slowly with stirring to a mixture of finely powdered $AlCl_3$ and benzene, stirring continued for 1 hr. at room temp. → *trans*-dibenzoylethylene. Y: 74%. F. e. s. J. B. Conant and R. E. Lutz, Am. Soc. *45*, 1303 (1923); s. a. N. Campbell and N. M. Khanna, Soc. *1949*, S33.

Sym. benzophenones

RCOR

816.

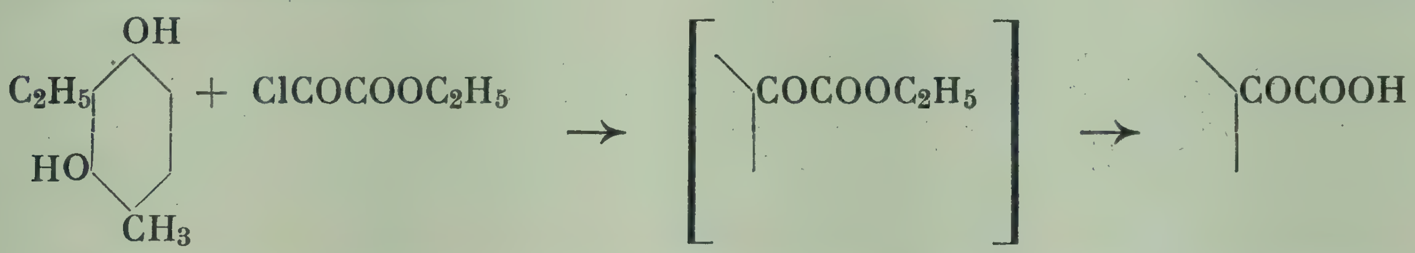


p-Fluorobenzene added to a mixture of dry CCl_4, anhydrous $AlCl_3$, and CS_2, kept 3 hrs. at room temp., ice added, excess CS_2 removed by steam distillation, and heating continued for 2 hrs. to hydrolyze the 4,4′-difluorobenzophenone dichloride → 4,4′-difluorobenzophenone. Y: 85%. F. e. s. J. P. Picard and C. W. Kearns, Can. J. Research *28B*, 56 (1950).

α-Ketocarboxylic acids

COCOOH

817.



$AlCl_3$ added gradually with stirring at 0° to a soln. of 2-ethyl-4-methylresorcinol and ethyl oxalyl chloride in nitrobenzene, allowed to stand 24 hrs. at room temp., decomposed with ice-HCl, and the nitrobenzene removed by steam distillation → 2,4-dihydroxy-3-ethyl-5-methyl-phenylglyoxylic acid. Y: 70%. F. e. s. R. D. Sprenger, P. M. Ruoff, and A. H. Frazer, Am. Soc. *72*, 2874 (1950).

Carboxylic acid amides from hydrocarbons
Synthesis with addition of 1 C-atom

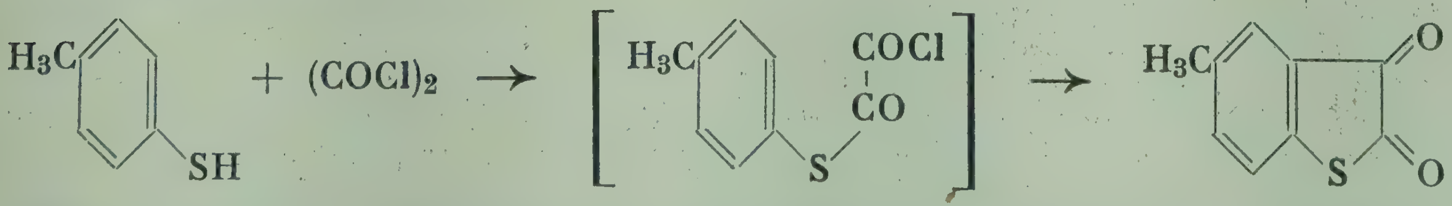
H → CON<

s. *5*, 607; subst. carboxylic acid amides s. J. H. Saunders, R. J. Slocombe, and E. E. Hardy, Am. Soc. *72*, 3312 (1950)

Thianaphthenequinones

○

818.



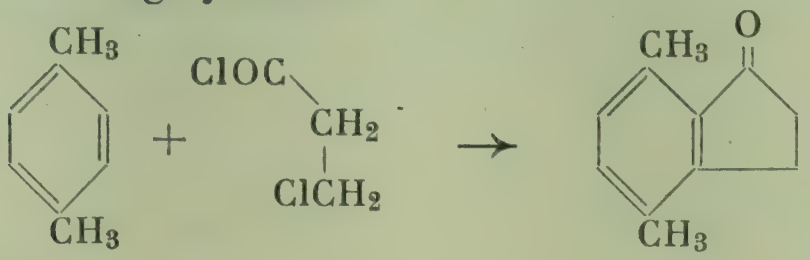
48 gm. of oxalyl chloride in dry ether added dropwise to 31 gm. p-thiocresol in ether, warmed on a steam bath, the ether evaporated, excess

oxalyl chloride removed in a vacuum desiccator over KOH, the residue dissolved in CS_2, cooled to 0°, $AlCl_3$ added, the temp. allowed to rise to room temp., then refluxed 0.5 hr. → 30 gm. 5-methylthianaphtenequinone (startg. m. f. 126). F. e. s. D. Papa, E. Schwenk, and H. F. Ginsberg, J. Org. Chem. *14*, 723 (1949).

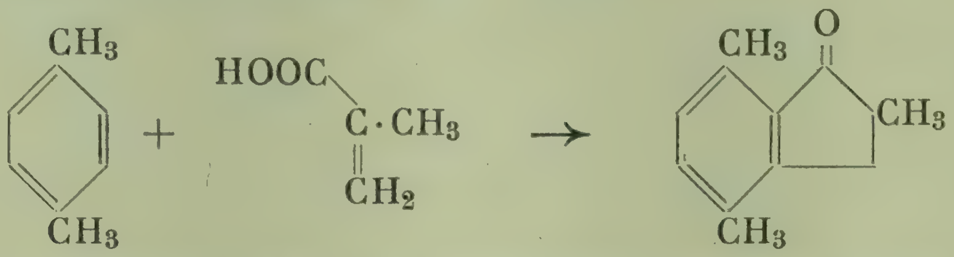
Aluminum chloride/sulfuric acid *$AlCl_3/H_2SO_4$*

One-step indanone ring synthesis

819.


CH3
CH3
ClOC
CH2
ClCH2
CH3
O
CH3

A soln. of β-chloropropionyl chloride and p-xylene in CS_2 added over 45 min. to $AlCl_3$ covered with CS_2, stirred 3 hrs. at room temp., CS_2 removed at the water-pump, concd. H_2SO_4 added, and heated 45 min. at 90° → 4,7-dimethyl-1-indanone. Y: 72.5%.

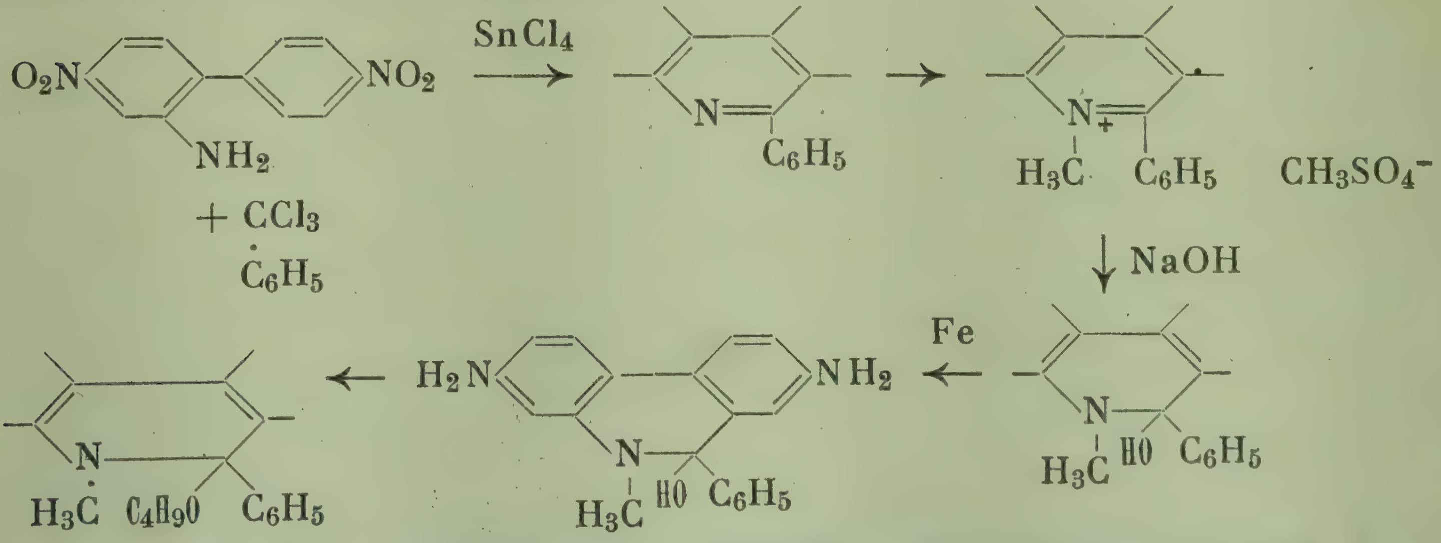

CH3
CH3
HOOC
C·CH3
CH2
CH3
O
CH3
CH3

A mixture of p-xylene and aq. 40%-methacrylic acid added to cold anhydrous liq. HF in a pressure reactor, shaken to aid in soln., and heated 6 hrs. at 90° → 2,4,7-trimethyl-1-indanone. Y: 62.1%. F. e. s. R. T. Hart and R. F. Tebbe, Am. Soc. *72*, 3286 (1950).

Stannic chloride *$SnCl_4$*

Shortened phenanthridine ring closure
6-Alkoxy-5,6-dihydrophenanthridines from phenanthridinium salts
Pseudobases
Amines from nitro compounds

820.

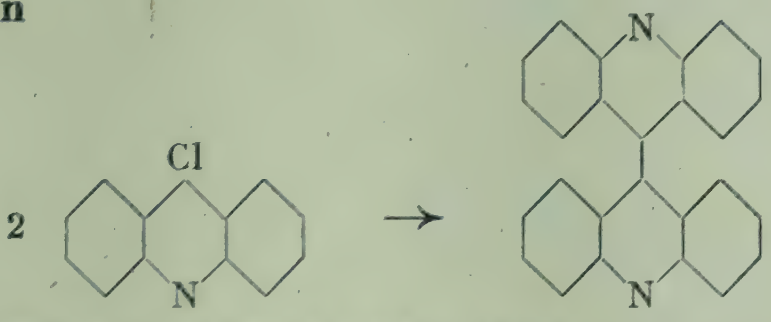

O2N
NO2
NH2
+ CCl3
C6H5
SnCl4
N
C6H5
N+
H3C
C6H5
CH3SO4−
NaOH
N
H3C
HO
C6H5
Fe
H2N
NH2
N
H3C
HO
C6H5
N
H3C
C4H9O
C6H5

A mixture of benzotrichloride and $SnCl_4$ added during 40 min. to a boiling soln. of 4,4′-dinitro-2-aminodiphenyl in dry nitrobenzene, refluxing continued for 1 hr., part of the nitrobenzene and $SnCl_4$ removed by distillation, dimethyl sulfate added at 190° during 2 min., kept 45 min. at ca. 180°, the residual nitrobenzene removed by steam distillation over a period of 7 hrs., partially neutralized at the boiling point with 2 *N* NaOH, filtered hot, added at ca. 80° during 7 min. to a boiling, vigorously stirred suspension of reduced Fe in water, stirred 45 min. at the boiling point, filtered, the filtrate treated with aq. NH_3, reboiled, on the next day filtered again, the filtrate stirred with butanol, then aq. NaOH added → 3,8-diamino-6-butoxy-6-phenyl-5-methyl-5,6-dihydrophenanthridine. Y: 67%. Limitations of the method for the ring closure s. H. J. Barber et al., J. Soc. Chem. Ind. *69*, 82 (1950); pseudobases s. a. B. Skinner, Soc. *1950*, 823.

Chromium sulfate *$CrSO_4$*

Dimerization 2 RHal → R·R

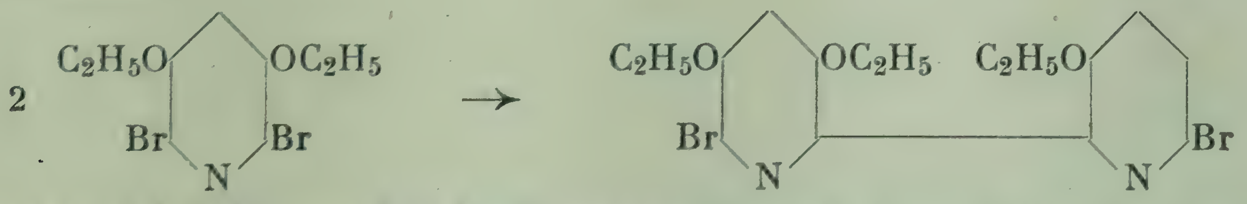
1.



A soln. of $CrSO_4$ in 0.1 *N* H_2SO_4 added, in an atmosphere of H_2, to a soln. of 5-chloroacridine in acetic acid at 20°, after 30 min. concd. H_2SO_4 and $K_2Cr_2O_7$ added, and boiled for 20 min. → 9,9′-biacridine. Y: 96%. R. Royer, Soc. *1949*, 1663.

Ferric bromide *$FeBr_3$*

2.

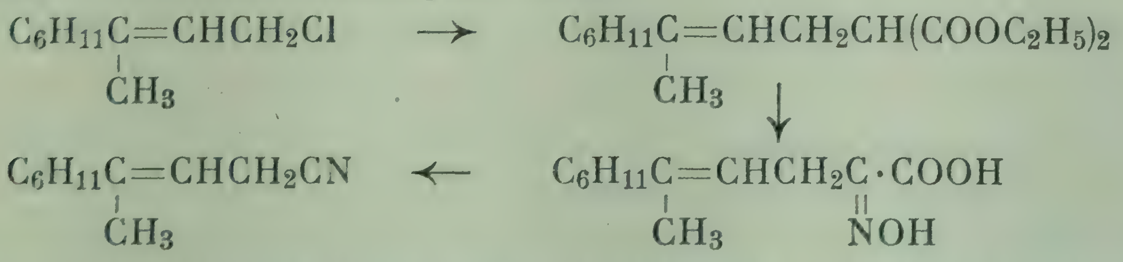


Dipyridyls. 2,6-Dibromo-3,5-diethoxypyridine shaken 6 hrs. in sunlight at 0° with a mixture of $FeBr_3$ and Br_2 → 6,6′-dibromo-3,3′,5,5′-tetraethoxy-2,2′-dipyridyl. Y: 95-100%. H. J. den Hertog and B. Mulder, R. *68*, 433 (1949).

Via intermediates *v.i.*

β,γ-Ethylenenitriles from β,γ-ethylenehalides via malonic esters and α-oximinocarboxylic acids ←

3.



$$\begin{tikzcd} \underset{CH_3}{C_6H_{11}C}{=}CHCH_2Cl \arrow[r] & \underset{CH_3}{C_6H_{11}C}{=}CHCH_2CH(COOC_2H_5)_2 \arrow[d] \\ \underset{CH_3}{C_6H_{11}C}{=}CHCH_2CN & \underset{CH_3}{C_6H_{11}C}{=}CHCH_2\underset{NOH}{C}\cdot COOH \arrow[l] \end{tikzcd}$$

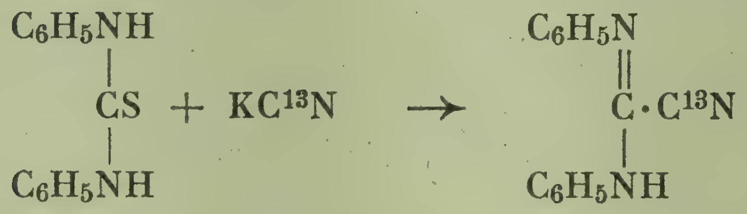
Ethyl geranylmalonate from geranyl chloride and ethyl malonate (Y: 50%) added slowly at 0° to a soln. of Na in ethanol, n-amyl nitrite added dropwise with vigorous stirring, ethanol removed under reduced pressure at 30°, mixed with crushed ice, acidified with aq. 25%-H_2SO_4, extracted with ether, washed with 10%-NaOH until colorless, and the aq. soln. thus obtained heated 15 min. on a steam bath, the dissolved ether being distilled off → crude α-oximinogeranylacetic acid (Y: 90%) suspended in light petroleum, acetic anhydride added slowly with stirring, and the resulting soln. stirred with water for 2 hrs. → geranyl cyanide (Y: 70%).—Other methods were inefficient. F. e. s. D. Barnard and L. Bateman, Soc. *1950*, 926.

Sulfur ↑ CC ⇅ S

Basic lead carbonate *$Pb(OH)_2 \cdot PbCO_3$*

Cyanoformamidines from thioureas ←
Labeled compounds

824.



$$\begin{array}{c}C_6H_5NH\\ |\\ CS\\ |\\ C_6H_5NH\end{array} + KC^{13}N \rightarrow \begin{array}{c}C_6H_5N\\ \|\\ C\cdot C^{13}N\\ |\\ C_6H_5NH\end{array}$$

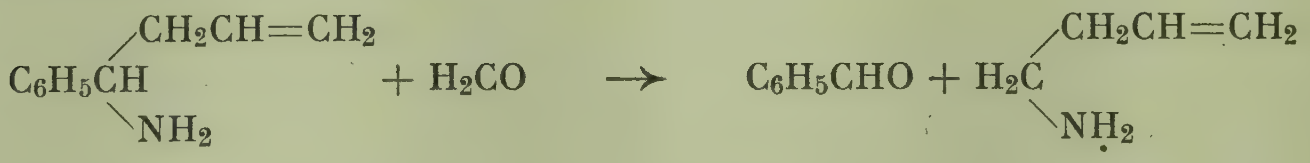
Basic Pb-carbonate, N,N′-diphenylthiourea, and 95%-alcohol added to aq. $KC^{13}N$, and warmed at 50-55° with stirring for ca. 1 hr., until a sample does not discolorize Pb-carbonate on short boiling → N,N′-diphenylcyanoformamidine (startg. m. f. 74). Crude Y: 90%. G. Ehrensvärd and R. Stjernholm, Acta Chem. Scand. *3*, 971 (1949).

Carbon ↑ CC ⇅ C

Without additional reagents *w.a.r.*

Allyl-aminomethane derivatives ←

825.



$$C_6H_5CH\begin{array}{l}\diagup CH_2CH{=}CH_2\\ \diagdown NH_2\end{array} + H_2CO \rightarrow C_6H_5CHO + H_2C\begin{array}{l}\diagup CH_2CH{=}CH_2\\ \diagdown NH_2\end{array}$$

A mixture of α-allylbenzylamine, 36-38%-formalin, and methanol refluxed 10 hrs., 6 *N* H_2SO_4 added, and steam-distilled → benzaldehyde (Y: 81%) and 3-butenylamine (crude Y: 56%). F. e. s. R. M. Horowitz and T. A. Geissman, Am. Soc. *72*, 1518 (1950).

Electrolysis ↯

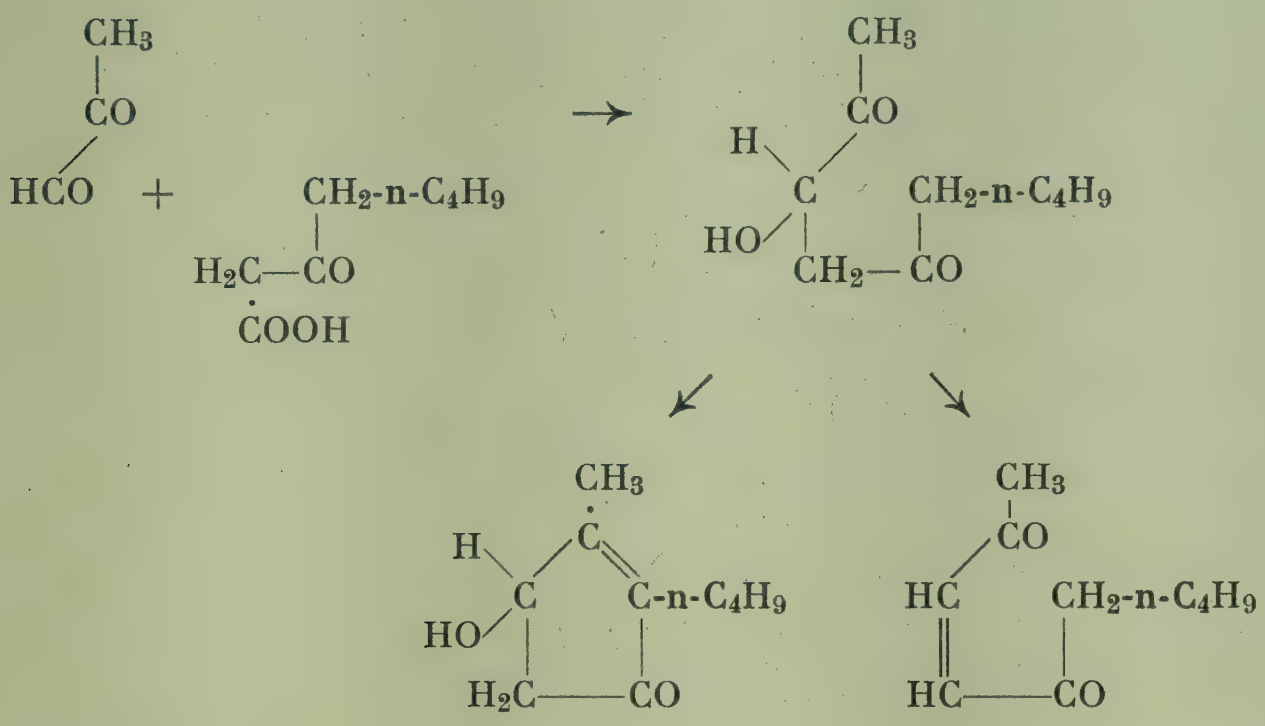
Ketones from carboxylic acids according to Kolbe RCOOH + HOOCR′ → R·R′

s. *1*, 715/6; s. a. R. P. Linstead et al., Soc. *1950*, 3326, 3331; retention of optical activity s. Soc. *1950*, 3333

Sodium hydroxide *NaOH*

α,β-Ethylene-γ-diketones and cyclopentenones from α-ketoaldehydes and β-ketocarboxylic acids via α-hydroxy-γ-diketones ←

826.



Na-β-oxocaprylate and pyruvaldehyde kept in very dil. aq. NaOH of pH 8 at room temp. for 2 days → 3-hydroxy-2,5-decanedione (Y: 65%)

shaken overnight with 2%-NaOH soln. under N_2 → d,l-dihydrocinerolone (Y: 63%).	treated with acetic anhydride and a little anhydrous Na-acetate, and heated 10 min. at 100° on the following day → 3-decene-2,5-dione (Y: ca. 100%).

F. e. s. M. S. Schechter, N. Green, and F. B. LaForge, Am. Soc. *71*, 3165 (1949).

Boron fluoride BF_3

Sym. ketones from carboxylic acid anhydrides

$RCO\cdot O\cdot OCR \rightarrow RCOR$

Self-condensation of carboxylic acid anhydrides

827. $CH_3[CH_2]_4CO\cdot O\cdot OC[CH_2]_4CH_3 \rightarrow CH_3[CH_2]_4CO[CH_2]_4CO_3$

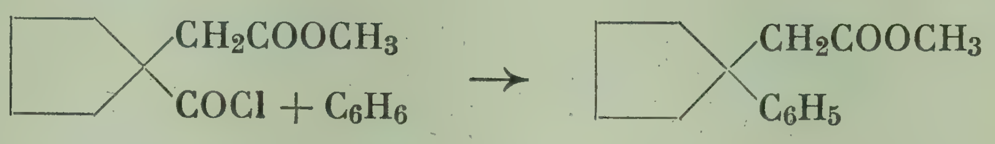
Caproic acid anhydride allowed to react with BF_3 at ca. 0° → di-n-amyl ketone. Y: 64%. F. e. s. E. H. Man and C. R. Hauser, Am. Soc. *72*, 3294 (1950).

Aluminum chloride *$AlCl_3$*

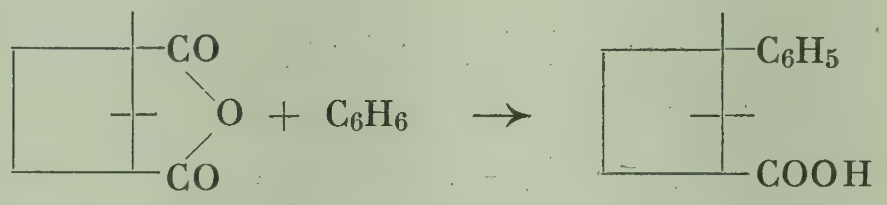
Synthesis of hydrocarbons from carboxylic acid chlorides ←

and of carboxylic acids from carboxylic acid anhydrides

828. In certain cases, arylation with loss of CO rather than ketone formation occurs in the presence of $AlCl_3$, e.g. with derivatives of tert. acids and benzene. However, derivatives of arylated tert. acids give cyclic ketones predominantly.



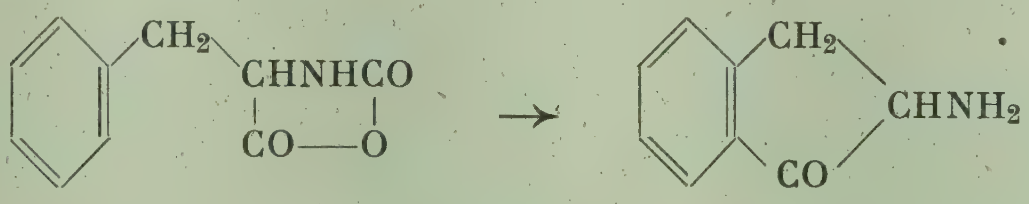
Methyl 1-chlorocarbonylcyclopentylacetate added to $AlCl_3$ and benzene below 10° → methyl 1-phenylcyclopentylacetate. Y: 78.9%. (Soc. *1949*, 1953).



$AlCl_3$ added in small portions to a vigorously stirred soln. of camphoric anhydride and benzene → 2-phenyl-1,1,2-trimethylcyclopentane-5-carboxylic acid. Y: 67% (Soc. *1949*, 1961). F. e. s. E. Rothstein and R. W. Saville, Soc. *1949*, 1946-61.

Aminoketones from N-carboxyaminocarboxylic acid anhydrides ←

829.

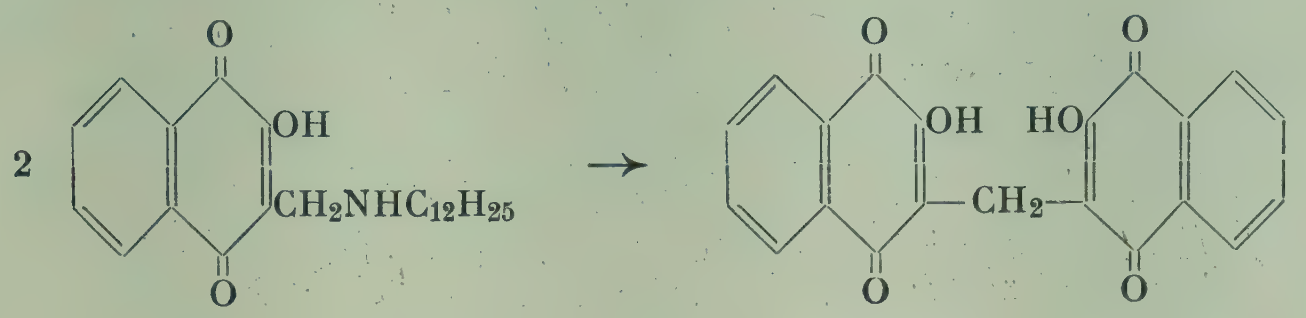


Powdered $AlCl_3$ added gradually with stirring at —10° to a suspension of anhydro-N-carboxyglycine in methylene dichloride, benzene added, the temp. allowed to rise to 10-20°, where it is maintained until gas evolution ceases → ω-aminoacetophenone. Y: 79% (isolated as picrate).—Similarly: Anhydro-N-carboxy-DL-β-phenylalanine → 2-aminoindanone. Y: 54% (isolated as picrate). F. e. s. F. S. Statham, Soc. *1951*, 213.

Acetic acid *CH_3COOH*

Methylene condensation ←

830.

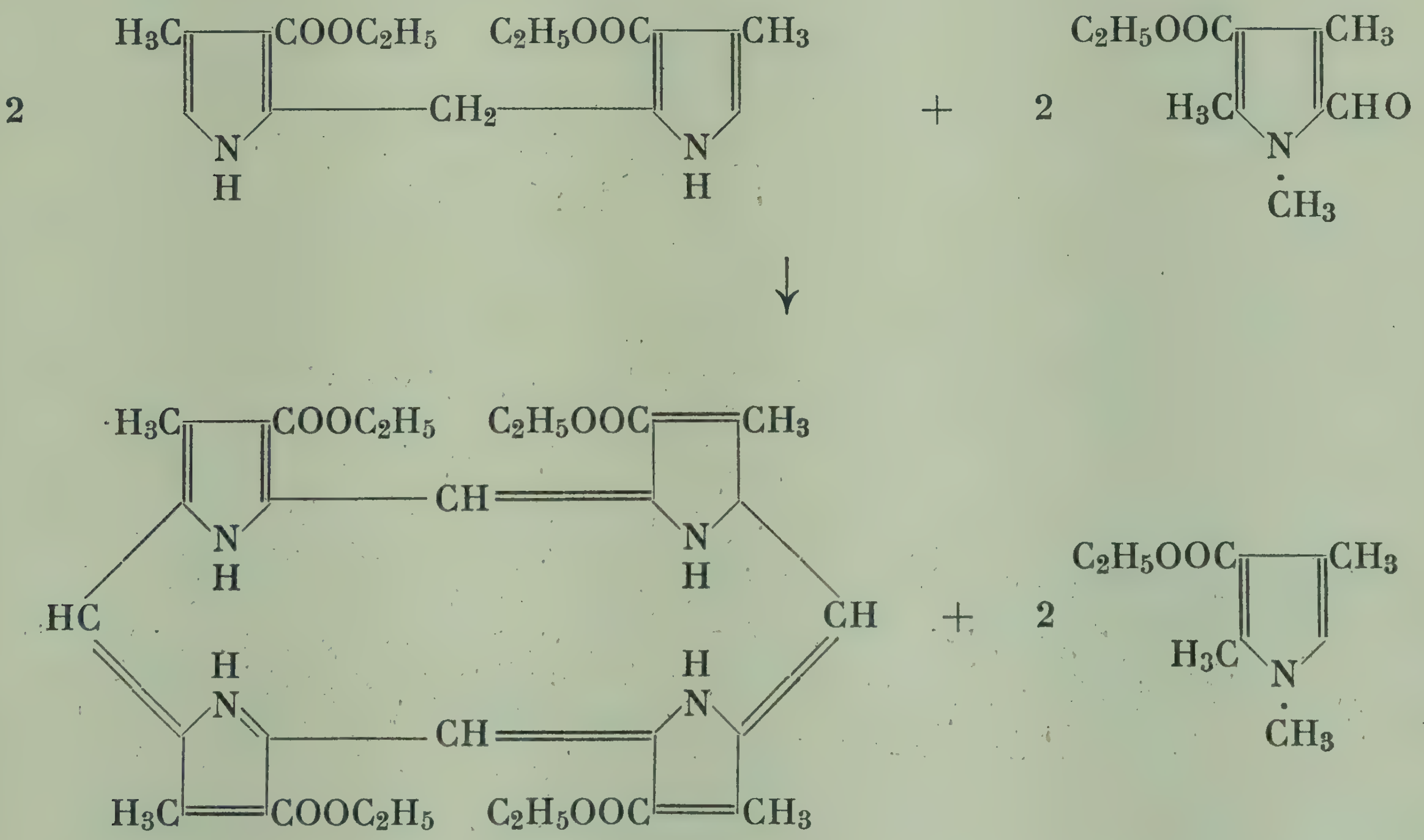


2-Hydroxy-3-dodecylaminomethyl-1,4-naphthoquinone warmed with glacial acetic acid → 3,3′-methylenebis-2-hydroxy-1,4-naphthoquinone. Y: 90%. C. E. Dalgliesh, Am. Soc. *71*, 1697 (1949).

Hydrochloric acid *HCl*

New synthesis of porphyrins ←

831.



A soln. of 3,3′-dicarbethoxy-4,4′-dimethyldipyrrylmethane and 1,2,4-trimethyl-3-carbethoxy-5-formylpyrrole in ether saturated with dry HCl at 0°, stoppered tightly, and allowed to stand 10 days in the dark at room temp. → 1,4,5,8-tetramethyl-2,3,6,7-tetracarbethoxyporphyrin. Y: up to 40%.—The pyrrole aldehyde appears to serve solely as the source of the methin groups. J. S. Andrews, A. H. Corwin, and A. G. Sharp, Am. Soc. *72*, 491 (1950).

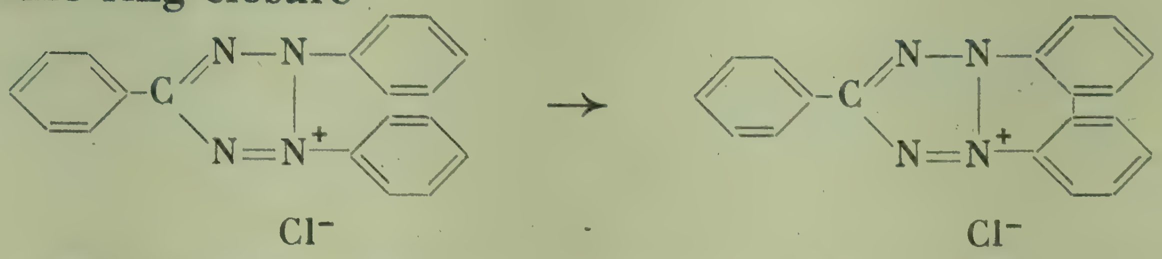
Elimination

Hydrogen ↑ CC ⇑ H

Without additional reagents *w.a.r.*

Pyridazine ring closure ○

832.



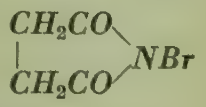
A soln. of triphenyltetrazolium chloride in abs. alcohol exposed to UV-light during 14 hrs. → 2,3-diphenylene-5-phenyltetrazolium chloride. Y: almost 100%. I. Hausser, D. Jerchel, and R. Kuhn, Chem. B. *82*, 195 (1949).

Aluminum chloride/hydrochloric acid *$AlCl_3/HCl$*

Scholl ring closure
Migration of alkyl groups

833. HCl catalyzes the Scholl reaction and the intramolecular migration of alkyl groups in phenol homologues, ar. ketones, and ar. hydroxyketones, in the presence of $AlCl_3$. These reactions do not occur, or occur at greatly reduced rates, when a stream of dry O_2 or N_2 is passed through the reaction mixture. E. s. G. Baddeley, Soc. *1950*, 994.

N-Bromosuccinimide



$$\begin{matrix} CH_2CO \\ | \\ CH_2CO \end{matrix} \!\!> NBr$$

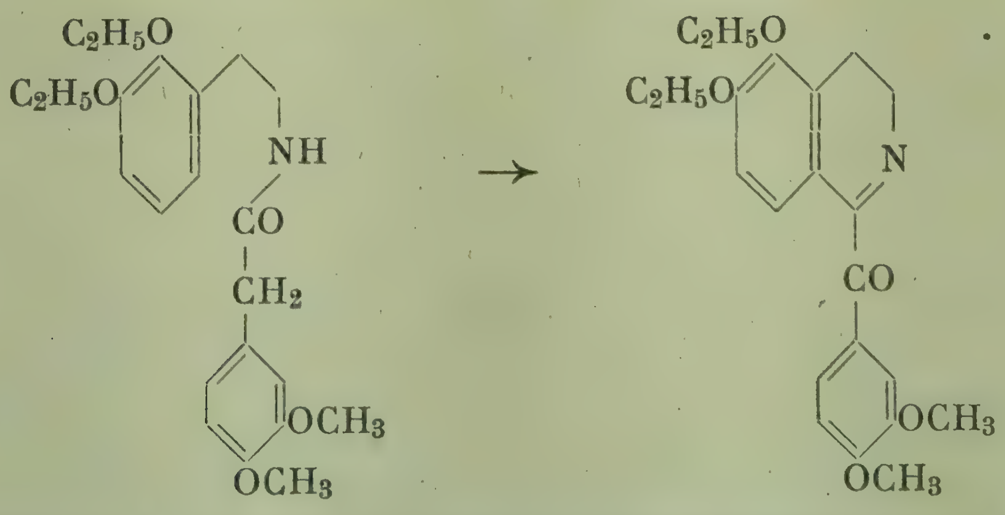
Dehydrogenation CHCH → C:C

s. *1*, 726; *2*, 757/8; O-heterocyclics s. T. A. Geissman, T. G. Halsall, and E. Hinreiner, Am. Soc. *72*, 4326 (1950); *73*, 782 (1951)

Phosphorus oxychloride *$POCl_3$*

Bischler-Napieralski ring closure with simultaneous oxidation ○

834.



$POCl_3$ added to a soln. of 3,4-dimethoxyphenylacetyl-β-(2,3-diethoxyphenyl)ethylamide in xylene, and refluxed 20 min. → 1-(3,4-dimethoxybenzoyl)-5,6-diethoxy-3,4-dihydroisoquinoline. Crude Y: 87.9%. F. e., without oxidation, s. G. Tsatsas, Bl. *1949*, 884.

Oxygen O_2

Dehydrogenation CHCH → C:C

s. *3*, 705; s. a. G. T. Gmitter and F. L. Benton, Am. Soc. *72*, 4586 (1950)

Sulfur *S*

s. *6*, 858; s. a. W. E. Bachmann and G. D. Johnson, Am. Soc. *71*, 3463 (1949)

Selenium dioxide SeO_2

α,β-Ethyleneketones from ketones

s. *4*, 807; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. *72*, 5530 (1950)

Chromic acid CrO_3

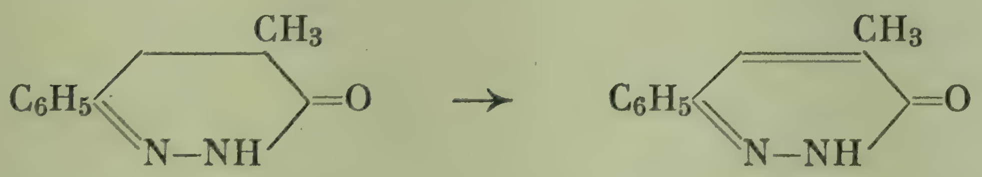
s. *6*, 709

9(H)-Pyrid[3.4-b]indoles

s. *6*, 780

Bromine *Br*

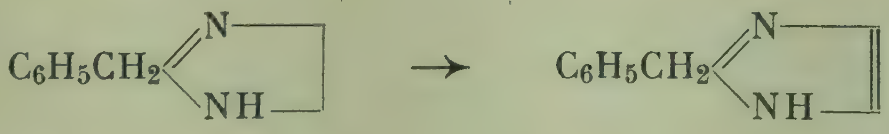
35.



Br_2 added dropwise to a soln. of 6-phenyl-4-methyl-pyridazinone in hot glacial acetic acid, then heated at 100° for 15 min. → 6-phenyl-4-methyl-3-pyridazone. Y: 83%. S. Dixon, H. Gregory, and L. F. Wiggins, Soc. *1949*, 2139; s. a. V. R. Mattox and E. C. Kendall, J. Biol. Chem. *185*, 601 (1950).

Cobalt-silica $Co\text{-}SiO_2$

36.



2-Benzyl-4,5-dihydroglyoxaline heated 45 min. at 250° with 40%-Co-kieselguhr catalyst until the H_2-evolution is complete, and the reaction product isolated as hydrochloride → 2-benzylglyoxalinium chloride. Y: 72%. P. Oxley and W. F. Short, Soc. *1950*, 859.

Nickel-chromium oxide *$Ni\text{-}Cr_2O_3$*

Benzene as hydrogen acceptor

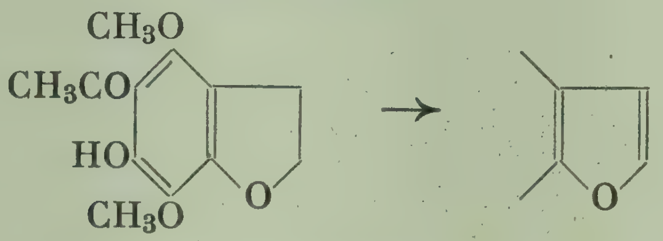
s. *4*, 811; also with other catalysts, preferably platinum s. Am. Soc. *71*, 2956-2964 (1949)

Palladium-carbon *Pd-C*

s. *1*, 729-31, 761; *2*, 765; *4*, 853; s. a. M. C. Kloetzel and F. L. Chubb, Am. Soc. *72*, 150 (1950); G. F. Woods, A. L. Van Artsdale, and F. T. Reed, Am. Soc. *72*, 3221 (1950); H. H. Günthard et al., Helv. *34*, 959 (1951)

Dehydrogenation in the vapor phase

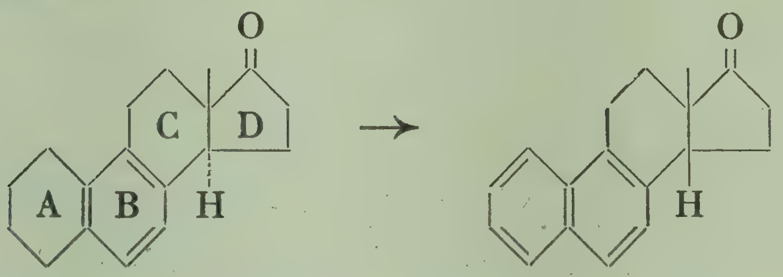
837.



1 gm. 6-hydroxy-4,7-dimethoxy-5-acetylcoumaran sublimed at 150°/10^{-4} mm. through a column of 30%-Pd-norit on glass wool, and the sublimation repeated with fresh catalyst → 0.8 gm. 6-hydroxy-4,7-dimethoxy-5-acetylcoumarone.—The success of the dehydrogenation depends on the nature of the catalyst. R. A. Baxter, G. R. Ramage, and J. A. Timson, Soc. *1949*, S30.

Dehydrogenation and epimerization
The action of palladium-on-charcoal catalyst on steroids

838.

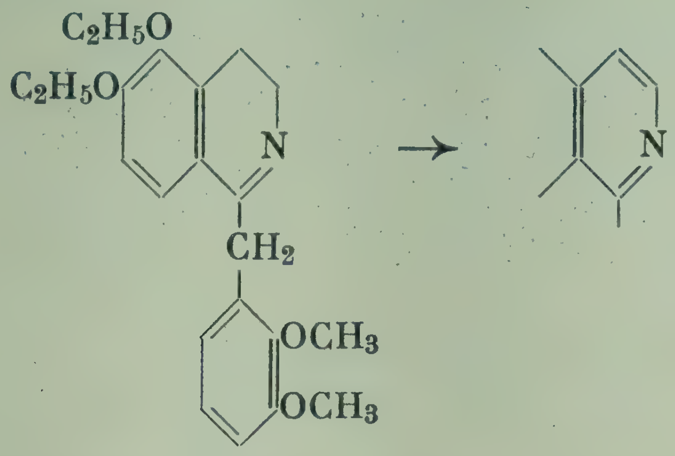


At 250°, three effects are obtained, depending on the compounds: (1) When the C-D ring juncture has the *trans*-configuration epimerization takes place at C_{14}. When the C-D ring juncture is *cis*, and when ring D is open in compounds of both configurations, no epimerization is observed. (2) When ring A (and/or B) is alicyclic it is aromatized. (3) A C_{17} hydroxyl group is dehydrogenated to a keto group.—At 350°, rings A, B, and C are dehydrogenated, and a cleavage of ring D occurs with loss of a carbon atom as CO_2 in such a manner that a 1-ethyl-2-methylphenanthrene structure results.—E: dl-1,2,3,4-Tetrahydrodesoxyequilenin and an equal weight of 5%-Pd-on-charcoal heated 8 min. at ca. 250° → dl-desoxyisoequilenin. Y: 86%. F. e. s. W. E. Bachmann and A. S. Dreiding, Am. Soc. *72*, 1323 (1950).

Palladium-pumice ←

Dehydrogenation

839.

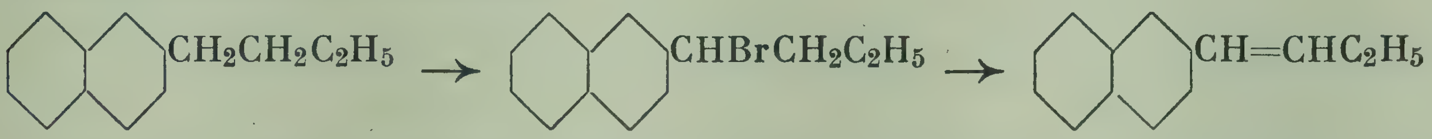


10%-Pd-on-pumice (prepn. s. original paper) added to a soln. of 1-(2,3-dimethoxybenzyl)-5,6-diethoxy-3,4-dihydroisoquinoline in tetralin, and boiled under CO_2 for 3 hrs. → 1-(2,3-dimethoxybenzyl)-5,6-diethoxy-3,4-isoquinoline. Y: 90%. F. e. s. G. Tsatsas, Bl. *1949*, 884.

Via intermediates *v.i.*

Ethylene derivatives from hydrocarbons via bromides

840.



A mixture of 2-n-butylnaphthalene, N-bromosuccinimide, and CCl_4 refluxed 6 hrs., and the crude bromo derivative heated 2 hrs. with quinoline at 150-160° → 1-(2-naphthyl)-1-butene. Y: 81%. G. B. Pickering and J. C. Smith, R. *69*, 535 (1950).

Oxygen ↑ CC ⇑ O

Without additional reagents *w.a.r.*

Thermal cleavage

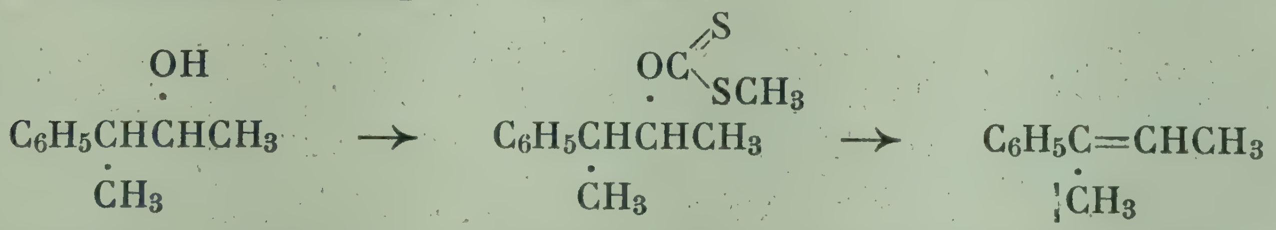
Ethylene derivatives from acetates CHC(OAc) → C:C

s. *2*, 768; *4*, 814; s. a. K. N. Campbell, J. O. Knobloch, and B. K. Campbell, Am. Soc. *72*, 4380 (1950); to *4*, 814 s. a. Am. Soc. *72*, 839 (1950)

Dehydration via xanthates CHC(OH) → C:C

cis-Elimination by Chugaev reaction

841.



$$C_6H_5\underset{CH_3}{CH}\overset{OH}{CH}CH_3 \rightarrow C_6H_5\underset{CH_3}{CH}\overset{OC(=S)SCH_3}{CH}CH_3 \rightarrow C_6H_5\underset{CH_3}{C}{=}CHCH_3$$

The Chugaev reaction is predominantly a *cis*-elimination reaction in an acyclic system.—3-Phenyl-2-butanol, K, and dry toluene refluxed 16 hrs., cooled, excess K removed, a large excess of CS_2 added, refluxed with stirring overnight, again cooled, methyl iodide added, and refluxed 4 hrs. → 3-phenyl-2-butyl xanthate (Y: 85%) heated at 180° with distillation of the olefin formed → 2-phenyl-2-butene (Y: 91%). D. J. Cram, Am. Soc. *71*, 3883 (1949); s. a. E. R. Alexander and A. Mudrak, Am. Soc. *72*, 3194 (1950).

Quinoline ring from enamines ○

s. *3*, 713; *5*, 614; optimum conditions s. W. J. Adams and D. H. Hey, Soc. *1950*, 3254

Naphthyridines from aminopyridines

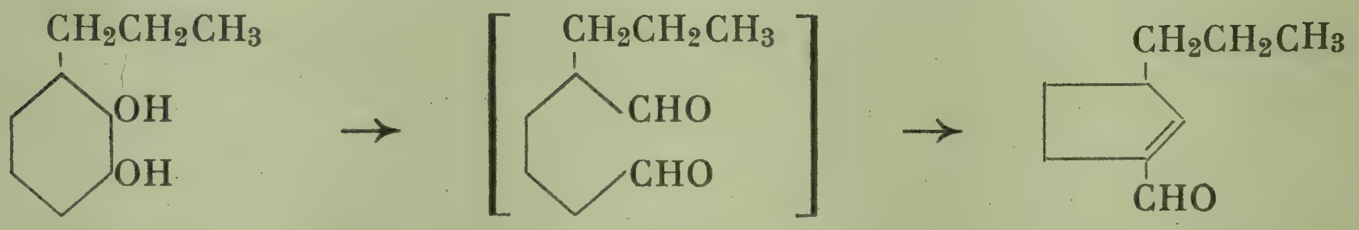
s. *5*, 355; s. a. C. R. Hauser and G. A. Reynolds, J. Org. Chem. *15*, 1224 (1950).

Quinoline ring via enamines
EMME method

s. *3*, 715; s. a. G. R. Loppin, J. Chem. Education *28*, 126 (1951)

1-Cyclopentenealdehydes ←
Ring contraction

842.



Pb-tetraacetate added over a period of 1 hr. under N_2 to a vigorously stirred mixture of 3-n-propylcyclohexane-1,2-diol and anhydrous K-carbonate in benzene, then stirred for an additional hr., the isolated, undistilled 2-propyladipic aldehyde (Y: 68% when distilled) heated 5 hrs. with distilled water at 110° in a bomb → 3-n-propyl-1-cyclopentenealdehyde. Y: 52%. F. e. s. J. English, Jr., and G. W. Barber, Am. Soc. *71*, 3310 (1949); s. a. E. B. Reid and J. F. Yost, Am. Soc. *72*, 5232 (1950).

Sodium *Na*

Acyloin condensation COCH(OH)

s. *4*, 816; s. a. F. Bouquet and C. Paquot, Bl. *1949*, 440; A. C. Cope and E. C. Herrick, Am. Soc. *72*, 983 (1950); J. C. Sheehan, R. C. O'Neill, and M. A. White, Am. Soc. *72*, 3376 (1950)

Sodium hydroxide *NaOH*

Cyclopentenones from
α-hydroxy-γ-diketones ○

s. *6*, 826

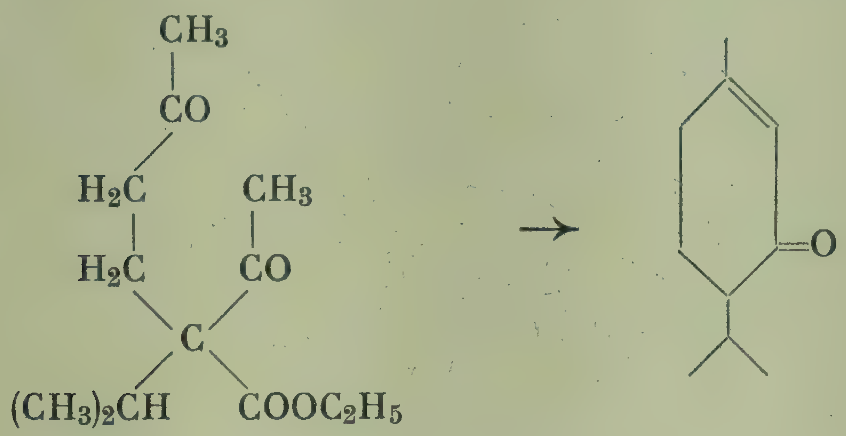
Anthrapyridones

s. *6*, 859

Potassium hydroxide/alcohol *KOH*

Cyclohexenones

843.



Ethyl 3-isopropylheptane-2,6-dione-3-carboxylate dropped into a 20% soln. of KOH in methanol, then boiled for 7 hrs. → piperitone. Y: 84.8%. F. e. s. H. Henecka, Chem. B. *82*, 112 (1949).

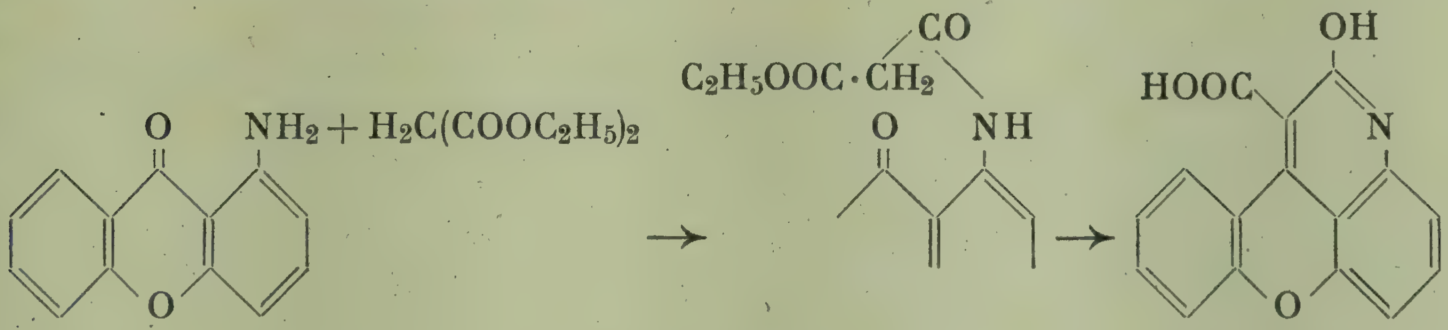
Sodium/alcohol *NaOR*

Dieckmann condensation

4-Piperidones s. *3*, 717; 3-piperidones s. A. W. D. Avison and A. L. Morrison, Soc. *1950*, 1471

Camps pyridone ring closure Dicarboxylic acid amide esters from dicarboxylic acid esters

844.



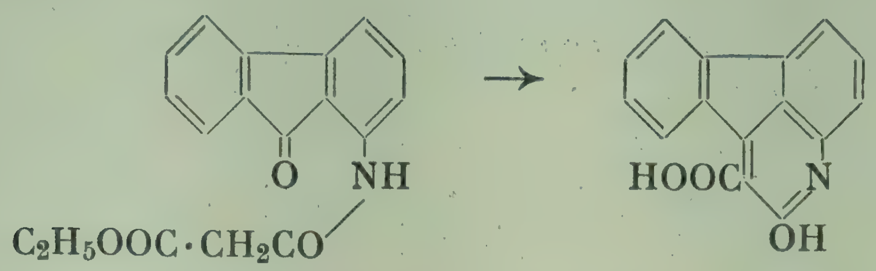
A soln. of 1-xanthoneamine and ethyl malonate boiled 20 min., then most of the ester removed by rapid distillation → 1-(carbethoxyacetamido)xanthone (Y: 86%), a suspension of this compound in alcohol treated at the boiling point during 15 min. with a soln. of Na in alcohol, then boiled for an additional 15 min. → ethyl 2-hydroxy[1]benzopyrano[4,2-de]quinoline-1-carboxylate (Y: 90%). F. e. s. C. F. Koelsch and F. J. Lucht, Am. Soc. *71*, 3556 (1949).

Azaindoles

s. *2*, 817; s. a. J. C. Clayton and J. Kenyon, Soc. *1950*, 2952

Sodium methoxide

4-Azafluoranthenes

845. 

A mechanically stirred soln. of 5 gm. 1-carbethoxyacetamidofluorenone in anhydrous nitrobenzene treated with powdered Na-methoxide, then heated 11 hrs. at 135-140° → 3.4 gm. 3-hydroxy-4-azafluoranthene-2-carboxylic acid. F. e. s. J. W. Cook and J. S. Moffatt, Soc. *1950,* 1160.

Sodium hydrogen carbonate *$NaHCO_3$*

N-Heterocondensed rings

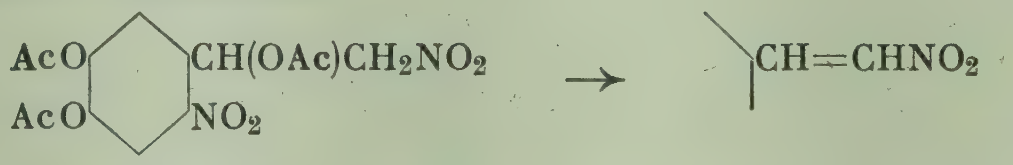
s. *3,* 726; pyrrolo 2.1-b thiazoles s. W. Traupel, M. Erne, and E. Sorkin, Helv. *33,* 1960 (1950)

Sodium acetate *CH_3COONa*

α,β-Ethylene-γ-diketones from α-hydroxy-γ-diketones CHC(OH) → C:C

s. *6,* 826

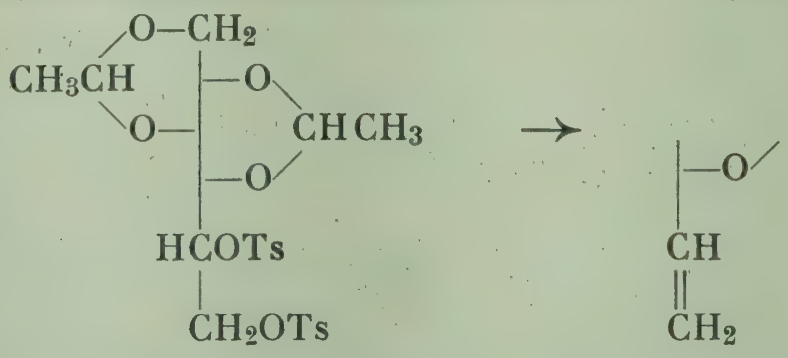
1,1-Nitroethylene derivatives from 1,2-nitroacoxy compounds CHC(OAc) → C:C

846. 

A mixture of 2-nitro-1-(2-nitro-4,5-diacetoxyphenyl)ethyl acetate, anhydrous Na-acetate, and acetic anhydride boiled 1-2 min. → β,2-dinitro-4,5-diacetoxystyrene. Y: 96%. F. e. s. H. Burton, J. A. Duffield, and P. F. G. Praill, Soc. *1950,* 1062.

Sodium iodide *NaI*

Glycals from di-p-toluenesulfonic acid esters C(OTs)C(OTs) → C:C

847. 

5,6-Ditosyl-1,3:2,4-diethylidenesorbitol, anhydrous NaI, and pure acetone heated 6 hrs. in a pressure bottle at 100° → 1,3:2,4-diethylidene-5,6-sorbitoleen. Y: 73%. F. e. s. P. Bladon and L. N. Owen, Soc. *1950,* 598.

Pyridine *C_5H_5N*

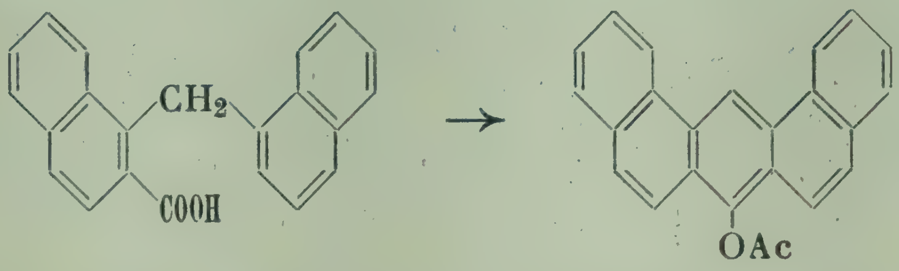
Ethylene derivatives from acoxy compounds CHC(OAc) → C:C

s. *6*, 864

Zinc chloride *$ZnCl_2$*

Anthracene ring ○

848.



A mixture of 1,1′-dinaphthylmethane-2-carboxylic acid, glacial acetic acid, acetic anhydride, and a little anhydrous $ZnCl_2$ refluxed for ca. 1 hr. → 10-acetoxy-1,2,7,8-dibenzanthracene. Y: 85%. J. W. Cook and E. F. M. Stephenson, Soc. *1949*, 842; method, see L. F. Fieser and E. B. Hershberg, Am. Soc. *59*, 1032 (1937); *60*, 1895 (1938).

Enediolethers from α-alkoxyacetals ←

849. $C_2H_5OCH_2CH(OC_2H_5)_2 \rightarrow C_2H_5OCH{=}CHOC_2H_5$

Ethoxyacetal dropped onto alumina pellets at 190° under a slight N_2-pressure → 1,2-diethoxyethylene. Y: 70%. S. M. McElvain and C. H. Stammer, Am. Soc. *73*, 915 (1951).

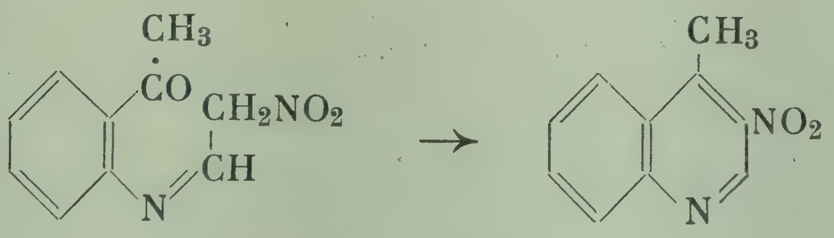
Alumina *Al_2O_3*

Dehydration CHC(OH) → C:C

s. *1*, 744; *3*, 730/1; s. a. D. T. Mowry and E. L. Ringwald, Am. Soc. *72*, 2037 (1950); I. A. Goodman and P. H. Wise, Am. Soc. *72*, 3076 (1950); V. N. Ipatieff, H. R. Appell, and H. Pines, Am. Soc. *72*, 4260 (1950)

3-Nitroquinolines ○

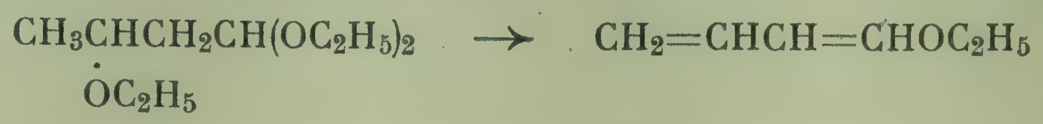
850.



o-(2-Nitroethylideneamino)acetophenones and their oximes are quantitatively cyclized by activated alumina, except in a few cases.—E: An acetone soln. of 2-(2-nitroethylideneamino)acetophenone treated with 10 parts of activated Al_2O_3, and left overnight → 3-nitrolepidine. F. e. s. K. Schofield and R. S. Theobald, Soc. *1950*, 395.

Aluminum phosphate water glass ←

Alkoxydienes from alkoxyacetals ←

851. 

$CH_3\underset{OC_2H_5}{CH}CH_2CH(OC_2H_5)_2 \rightarrow CH_2{=}CHCH{=}CHOC_2H_5$

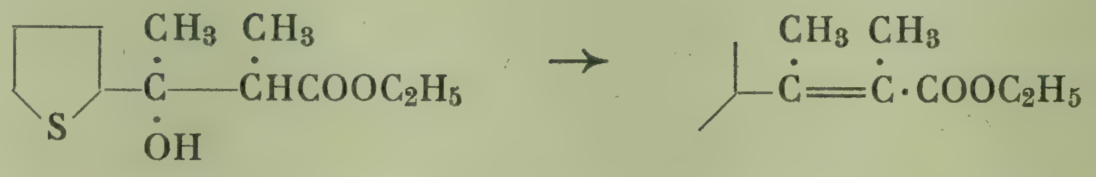
1,1,3-Triethoxybutane distilled through $AlPO_4$-water glass at 300°/10 mm. over a period of 1 hr. → 1-ethoxy-1,3-butadiene. Y: 82%. F. e., catalysts, and reaction conditions s. W. Flaig, A. *568*, 1 (1950).

Acetic acid *CH_3COOH*

Dehydration CHC(OH) → C:C

s. *6*, 628

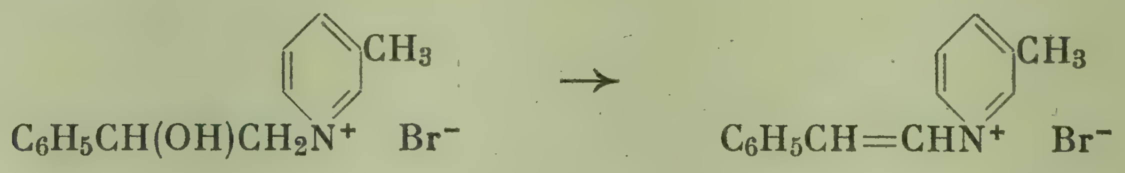
Oxalic acid *$(COOH)_2$*

852. 

Ethyl α,β-dimethyl-β-hydroxy-β-(2-thienyl)propionate refluxed with 6% aq. oxalic acid for 3-6 hrs. → ethyl α,β-dimethyl-β-(2-thienyl)-acrylate. Y: almost 100%. Other dehydration reagents caused the formation of tarry by-products. F. e. s. R. E. Miller and F. F. Nord, J. Org. Chem. *15*, 89 (1950); s. a. E. D. Bergmann, R. Pappo, and D. Ginsburg, Soc. *1950*, 1369.

s. a. *3*, 734; C. C. Price and J. A. Pappalardo, Am. Soc. *72*, 2613 (1950)

Benzoyl chloride *C_6H_5COCl*

853. 

A mixture of 1-(2-phenyl-2-hydroxyethyl)-3-picolinium bromide and benzoyl chloride heated 1 hr. at 190-200° → 1-styryl-3-picolinium bromide. Y: 83%. F. e. s. L. C. King and W. B. Brownell, Am. Soc. *72*, 2507 (1950).

Phosphorus pentoxide *P_2O_5*

s. *2*, 783; s. a. R. L. Frank and R. E. Berry, Am. Soc. *72*, 2985 (1950); styrenes E. T. McBee and R. A. Sanford, Am. Soc. *72*, 4053 (1950)

Phosphorus pentoxide/phosphoric acid *P_2O_5/H_3PO_4*

Cyclic ketones from carboxylic acids ○

s. *5*, 622; s. a. R. C. Gilmore, Jr., and W. J. Horton, Am. Soc. *73*, 1411 (1951)

Phosphoric acid *H_3PO_4*

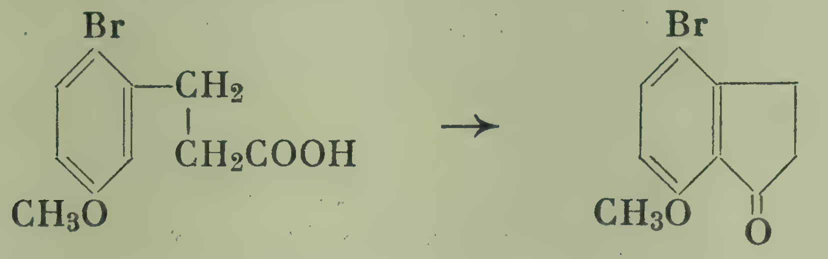
Dehydration of stereoisomeric cyclic alcohols $CHC(OH) \rightarrow C:C$

s. *6*, 867

Polyphosphoric acid *$H(PO_3H)_xOH$*

Cyclic ketones from carboxylic acids ○

854.

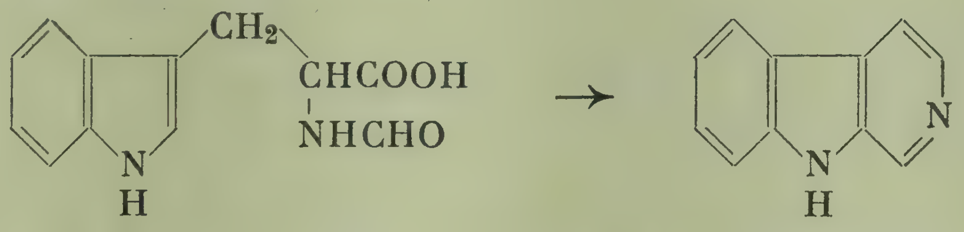


A mixture of 2-bromo-5-methoxyhydrocinnamic acid and polyphosphoric acid heated with vigorous stirring at 90-105° for 5 min. → 4-bromo-7-methoxy-1-indanone. Crude Y: 76%. F. e. s. H. R. Snyder and F. X. Werber, Am. Soc. *72*, 2965 (1950).

Polyphosphoric acid/phosphorus oxychloride *$H(PO_3H)_xOH/POCl_3$*

Bischler-Napieralski ring closure

855.



A mixture of N-formyl-d,l-tryptophan, polyphosphoric acid, and $POCl_3$ heated 80 min. in an oil-bath at 125° with vigorous stirring → norharman. Y: 36%.—In certain cases, the mixture of polyphosphoric acid and $POCl_3$ is the only catalyst to effect cyclization. F. e. s. H. R. Snyder and F. X. Werber, Am. Soc. *72*, 2962 (1950).

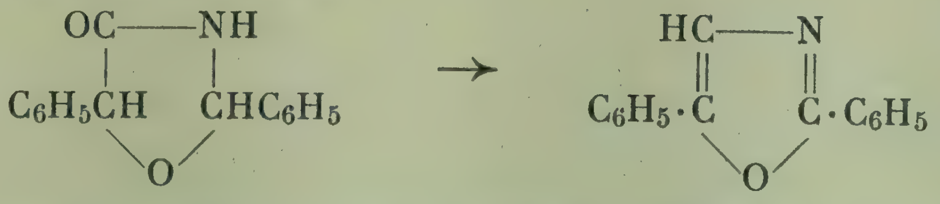
Phosphorus oxychloride *$POCl_3$*

3,4-Dihydroisoquinolines

s. *2*, 788; s. a. L. Marion, L. Lemay, and R. Ayotte, Can. J. Research *28B*, 21 (1950); E. R. Shepard and J. F. Noth, Am. Soc. *72*, 4364 (1950); W. Reese and W. M. Eareckson, 3rd, Am. Soc. *72*, 5195 (1950)

Oxazoles from oxazolidones ←

856.



Crude 2 gm. 2,5-diphenyl-4-oxazolidone warmed with $POCl_3$ for 0.5 hr. at 85-90°, $POCl_3$ removed at low pressure, the residue triturated with ethereal 1%-HCl, collected, and shaken with water and ether → 1.5 gm. 2,5-diphenyloxazole. F. e. s. J. W. and R. H. Cornforth, Soc. *1949*, 1028.

Sodium hydrogen sulfate $NaHSO_4$

Enolethers from acetals $CHC(OR)_2 \rightarrow C:C(OR)$

s. *6*, 182; s. a. M. G. Voronkov, Ж. *20*, 2060 (1950); C. A. *45*, 5607h

Sulfuric acid H_2SO_4

Dehydration of alcohols $CHC(OH) \rightarrow C:C$

s. *5*, 627; with 85%-H_2SO_4 s. D. W. Adamson and J. W. Billinghurst, Soc. *1950*, 1039; with 30%-H_2SO_4 s. E. D. Bergmann, Am. Soc. *73*, 1218 (1951)

Isocyclics from alcohols ○

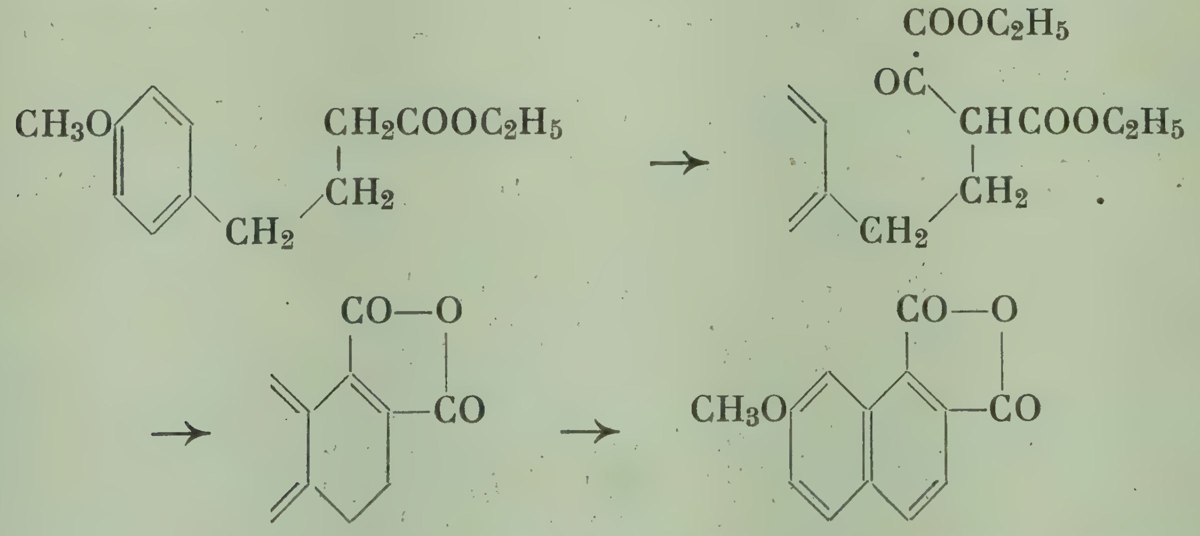
857. Tert. alcohols are cyclized more easily than sec. alcohols. E. for both types s. J. Colonge and L. Pichat, Bl. *1949*, 855; s. a. H. W. D. Stubbs and S. H. Tucker, Soc. *1950*, 3288.

Cyclic ketones from carboxylic acids

s. *2*, 796/7; s. a. M. C. Kloetzel, R. P. Dayton, and H. L. Herzog, Am Soc. *72*, 273 (1950)

Dicarboxylic acid anhydrides from carboxylic acid esters via α-keto-β-dicarboxylic acid esters
Bougault ring closure
Dehydrogenation

858.



The K salt of ethyl α-(ethoxalyl)-γ-(p-methoxyphenyl) butyrate, prepared from ethyl γ-(p-methoxyphenyl)butyrate and ethyl oxalate in the presence of K-ethoxide in ether, added in small portions with stirring to ice-salt-cooled 60%-H_2SO_4, heated 15 min. on a steam bath.

cooled, treated with 80%-H_2SO_4, and heated 15 min. longer → 7-methoxy-3,4-dihydronaphthalene-1,2-dicarboxylic acid anhydride. Y: 77%. —By using H_2SO_4 just strong enough to effect the cyclization, aromatization in some cases can be prevented or at least minimized. Aromatization can be effected easily and in good yields with sulfur. F. e. s. L. F. Fieser and E. B. Hershberg, Am. Soc. *58,* 2314 (1936); s. a. W. G. Dauben and M. Tanabe, Am. Soc. *71,* 2877 (1949).

Xanthylium salts

s. *6,* 162

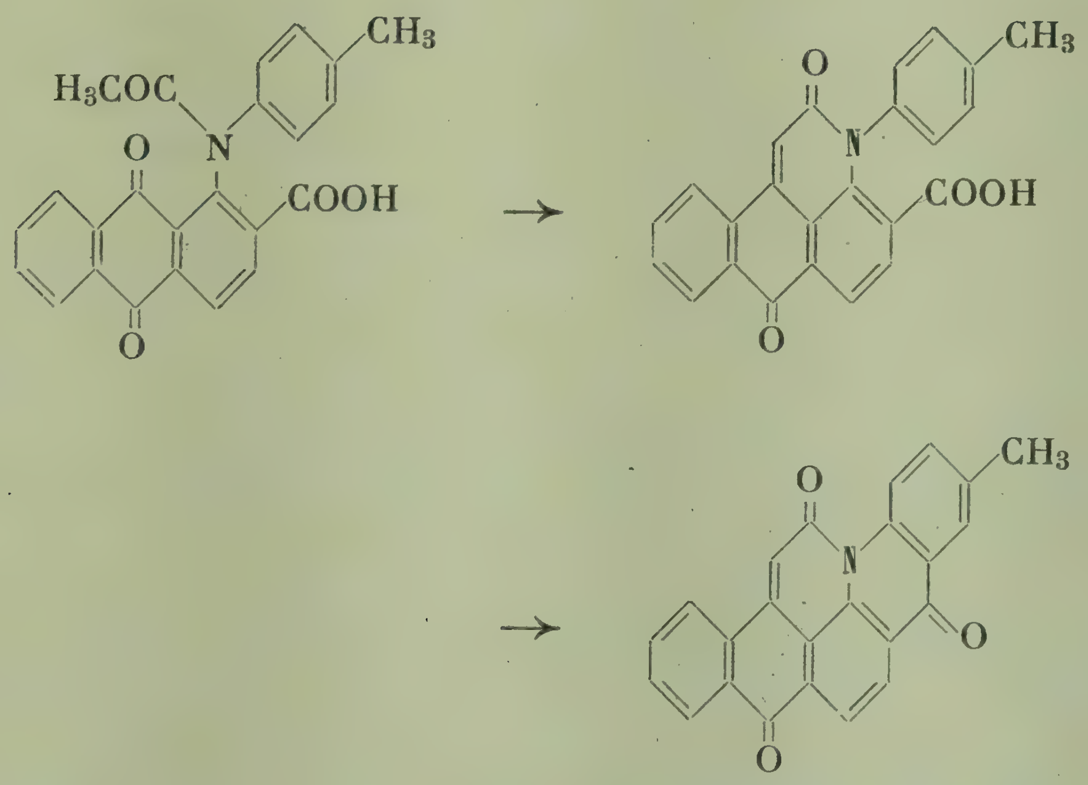
Quinoline ring from azomethines according to Combes

s. *4,* 835; s. a. D. H. Hey and J. M. Williams, Soc. *1950,* 1678; R. Adams and J. Campbell, Am. Soc. *72,* 1021 (1950)

Chlorosulfonic acid $ClSO_3H$

Anthrapyridonacridones via anthrapyridones

59.

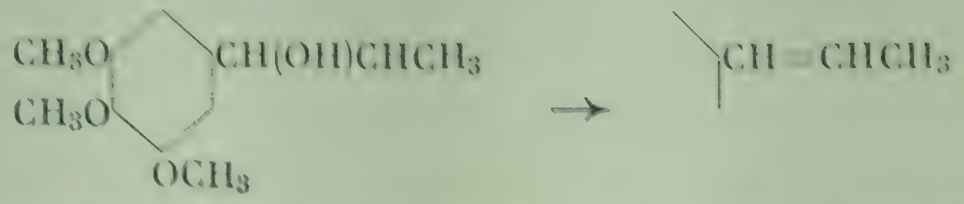


1-(N-Acetyl-p-tolylamino)anthraquinone-2-carboxylic acid boiled 10 hrs. with 0.8%-NaOH → N-(p-tolyl)-1,9-anthrapyridone-2-carboxylic acid (Y: 96%) warmed at 40-45° with chlorosulfonic acid for 2 hrs. → 4″-methyl-1,9-anthrapyridonacridone (Y: 98%). F. e. s. A. M. Lukin and P. M. Aronovich, Ж. *19,* 358 (1949); C. A. *44,* 1079h.

Iodine *I*

Dehydration of alcohols CHC(OH) → C:C

860.



3,4,5-Trimethoxyphenylethylcarbinol heated with a crystal of iodine under distillation conditions at diminished pressure → isoelemicin. Y: 85-87%.—Other methods (s. original paper) were less satisfactory. J. W. Cook, T. Y. Johnston, and J. D. Loudon, Soc. *1950*, 537.

Hydrofluoric acid *HF*

Cyclic ketones from carboxylic acids ○

s. *1*, 758-61; *2*, 801; s. a. M. F. Ansell and D. H. Hey, Soc. *1950*, 2871

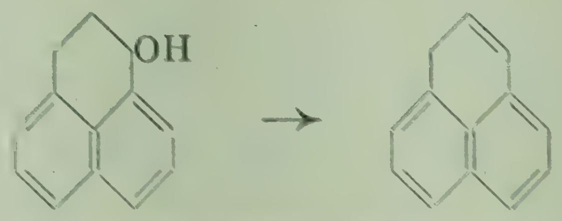
Cyclic ketones from carboxylic acids and carboxylic acid chlorides

861. The formation of cyclic ketones from carboxylic acids with HF or their chlorides with $AlCl_3$ can give markedly contrasting results. Syntheses of indan-1-one-carboxylic acids from β-arylsubst. glutaric acids, s. D. H. Hey and D. H. Kohn, Soc. *1949*, 3177; s. a. C. D. Gutsche, Am. Soc. *73*, 786 (1951).

Hydrochloric acid *HCl*

Dehydration CHC(OH) → C:C

862.

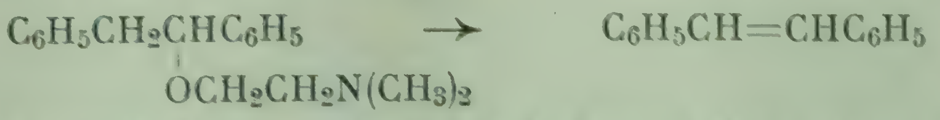


Perinaphthanol-7 in HCl-abs. alcohol refluxed 15 min. → perinaphthene. Y: 65-85%. — Other methods were not successful. V. Boekelheide and C. E. Larrabee, Am. Soc. *72*, 1245 (1950); f. e. s. Am. Soc. *72*, 1240 (1950).

with simultaneous esterification
s. *6*, 689

Ethylene derivatives from ethers CHC(OR) → C:C

863.

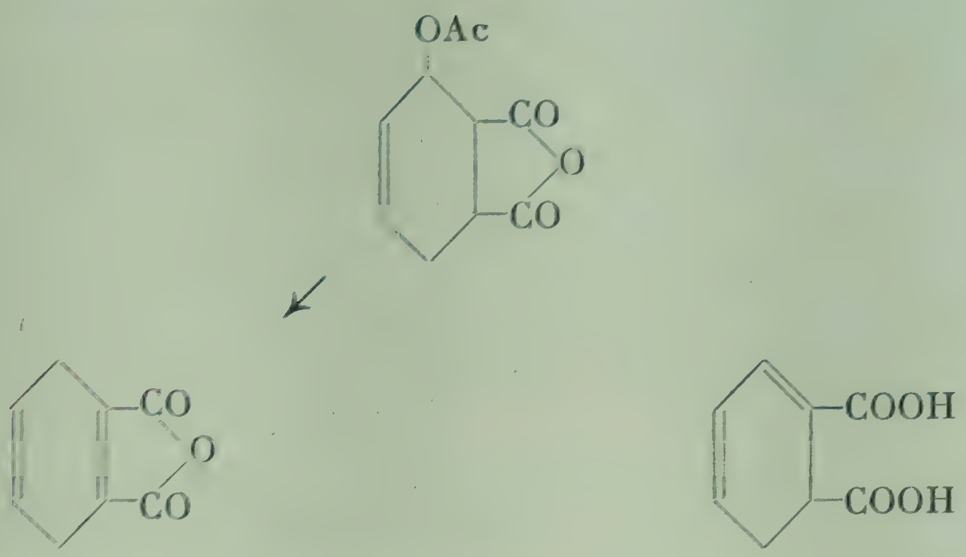


$$\underset{OCH_2CH_2N(CH_3)_2}{C_6H_5CH_2CHC_6H_5} \rightarrow C_6H_5CH{=}CHC_6H_5$$

A soln. of β-dimethylaminoethyl 1,2-diphenylethyl ether in 20%-HCl heated 1 hr. on a steam bath → stilbene. Crude Y: ca. 95%. N. Sperber, R. Fricano, and D. Papa, Am. Soc. *72*, 3068 (1950).

Ethylene derivatives from acoxy compounds with rearrangement ←

64.



3-Acetoxy-1,2,3,6-tetrahydrophthalic anhydride (prepn. s. 695)

heated with pyridine on a water bath for 10 min. → 3,6-dihydrophthalic anhydride. Y: almost 100%.

(50 gm.) refluxed with concd. HCl → 33 gm. 2,3-dihydrophthalic acid.

Also one-step syntheses of 3,6-dihydrophthalic anhydride from crotonaldehyde and maleic anhydride (cf. 695) s. W. Flaig, A. *568,* 1 (1950).

Ar. amines from hydroaromatic oximes ←
Dehydroisomerization

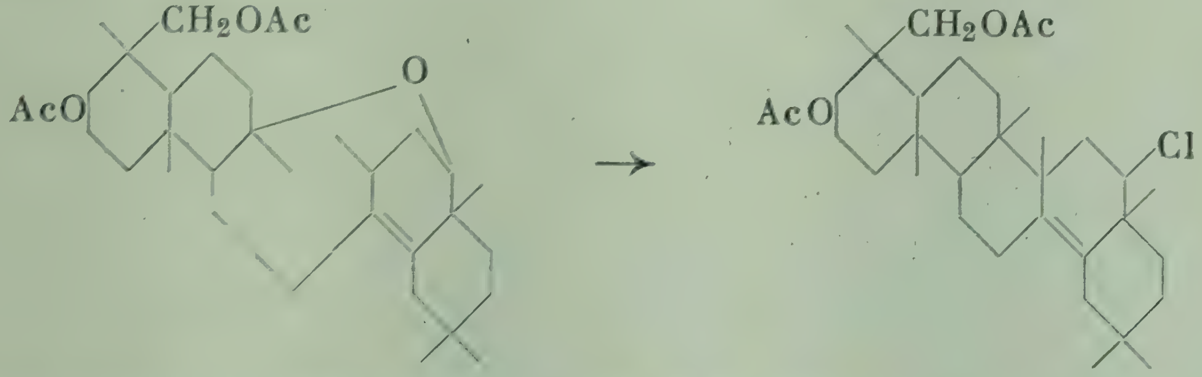
s. *2,* 778; s. a. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. *15,* 1197 (1950)

Isocyclics from ketones ○

s. *2,* 697; s. a. A. C. Cope, F. S. Fawcett, and G. Munn, Am. Soc. *72,* 3399, 3405 (1950)

Isocyclics from O-heterocyclics ←

65.



HCl-gas introduced at 95° into a soln. of soysapogenol-D diacetate in acetic anhydride for 2 hrs. → pentacyclic diacetoxychloro derivative. Y: 91%. A. Meyer, O. Jeger, and L. Ruzicka, Helv. *33,* 687 (1950).

Hydrochloric acid/acetic acid HCl/CH_3COOH

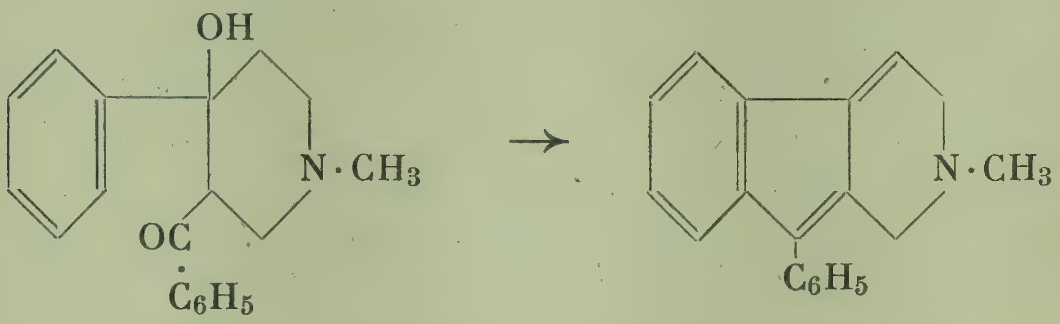
Dehydration CHC(OH) → C:C

s. *1,* 534, 764; ethylene amines s. D. W. Adamson, P. A. Barrett, and S. Wilkinson, Soc. *1951,* 52

Hydrobromic acid *HBr*

1H-Indeno[2.1-c]pyridines ○

866.



750 gm. 1-methyl-3-benzoyl-4-hydroxy-4-phenylpiperidine and 48%-HBr distilled over a period of ca. 1 hr., then the residue worked up →700-720 gm. 2-methyl-9-phenyl-2,3-dihydro-1-pyridindene hydrobromide. F. e. s. J. T. Plati and W. Wenner, J. Org. Chem. *15,* 209 (1950).

Hydrobromic acid/acetic acid HBr/CH_3COOH

Isocyclics from ketones

s. *5,* 642; s. a. Am. Soc. *72,* 277 (1950)

Via intermediates *v.i.*

Dehydration of stereoisomeric cyclic alcohols CHC(OH) → C:C

867. In contrast to the H_3PO_4-catalyzed dehydration of *cis-* and *trans*-2-phenylcyclohexanols, the thermal decomposition of their acetates or methyl xanthates involves the preferential elimination of a *cis-β*-H-atom. E. s. E. R. Alexander and A. Mudrak, Am. Soc. *72,* 1810 (1950).

Cyclic ketones from carboxylic acids ○

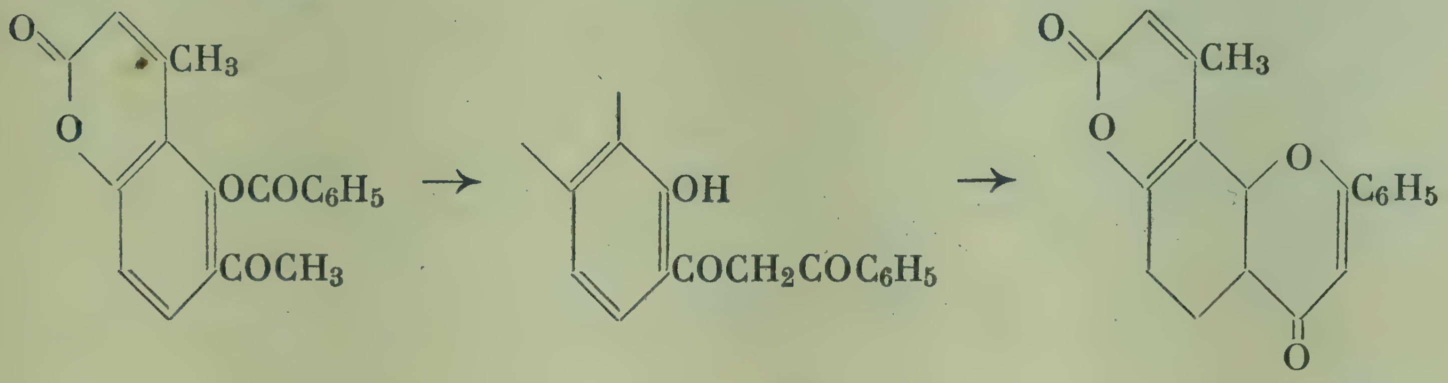
s. *1,* 778-80; *2,* 808; *4,* 841; *5,* 652/3

Naphtho[1.8-bc]thiapyrans

s. *6,* 889

o-Hydroxy-β-diketones from o-acoxyketones
Baker-Venkataraman transformation
Chrome ring

868.



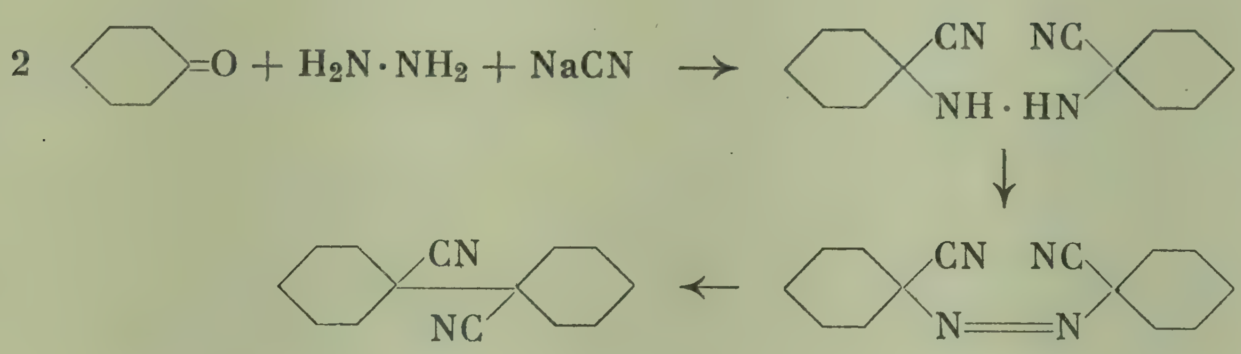
A mixture of 5-benzoyloxy-6-acetyl-4-methylcoumarin, ethyl Na-acetoacetate, and pyridine refluxed 20 min., and kept at room temp. for 12 hrs. → 5-hydroxy-6-benzoylacetyl-4-methylcoumarin (Y: almost 100%) dissolved in acetic acid containing 50% HBr, then diluted with water → 2′-phenyl-4-methylchromono[7′,8′,6,5]-2-pyrone (Y: almost 100%). F. e., also one-step preparation, s. T. S. Wheeler et al., Soc. *1949*, 1915; also transformation with KOH/pyridine and ring closure with HCl and H_2SO_4 s. Soc. *1950*, 340, 1252, 1925; W. Baker and F. Glockling, Soc. *1950*, 2759.

Nitrogen ↑ CC ⇑ N

Without additional reagents *w.a.r.*

Sym. α-dinitriles from ketones via sym. hydrazodinitriles and sym. azodinitriles
Dimerization ←

869.



Cyclohexanone, hydrazine sulfate, and NaCN in water shaken at room temp. for 2 days → 1,1′-hydrazobis(cyclohexenecarbonitrile) (Y: 95%) dissolved in HCl-alcohol-water, and Br_2-water added until a permanent yellow color results → 1,1′-azobis(cyclohexanecarbonitrile) (Y: 92%) heated in small quantities at 120° in a N_2-stream for 1 hr. → 1,1′-dicyanobicyclohexyl (Y: 98%). F. e. s. C. G. Overberger, M. T. O'Shaughnessy, and H. Shalit, Am. Soc. *71*, 2661 (1949).

Potassium hydroxide *KOH*

Hofmann degradation ←
Ethylene derivatives from amines
s. *6*, 722

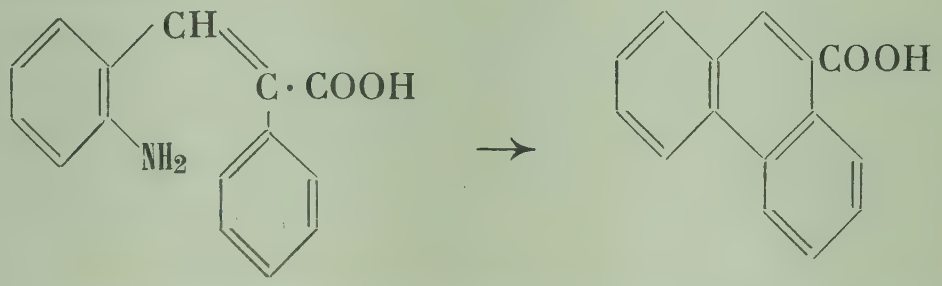
Sodium nitrite $NaNO_2$

Ring closure by diazo coupling ○
s. *2*, 810; discussion s. DeLos F. DeTar and S.V. Sagmanli, Am. Soc. *72*, 965 (1950)

Copper *Cu*

Pschorr ring closure

870.

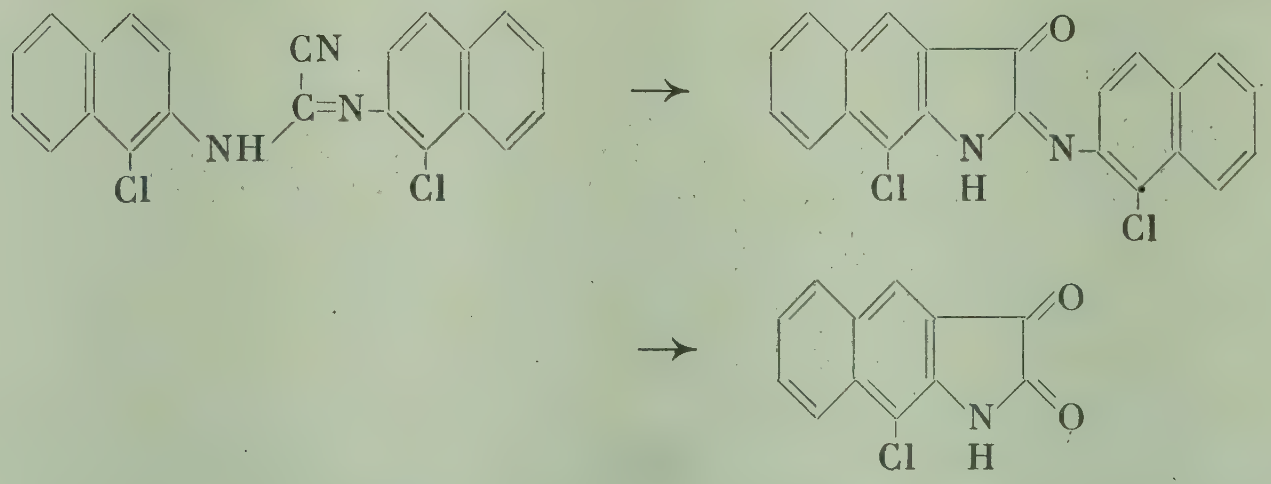


Isoamyl nitrite added dropwise with shaking at 0° to a suspension of o-amino-α-phenylcinnamic acid hydrochloride (from the acid and dry HCl) in alcohol, allowed to stand for 0.5 hr., ether added, filtered, and the solid diazonium chloride decomposed in the course of 1 min. under acetone in the presence of a small amount of Cu-powder → phenanthrene-9-carboxylic acid. Y: 81%. F. methods, discussion, and e. s. D. H. Hey and J. M. Osbond, Soc. *1949*, 3164, 3172; s. a. E. Schlittler and A. Lindemann, Helv. *32*, 1880 (1949); P. Block, Jr., Am. Soc. *72*, 5641 (1950).

Aluminum chloride/sodium chloride $AlCl_3/NaCl$

Isatins from amidines via 2-iminoisatins

871.

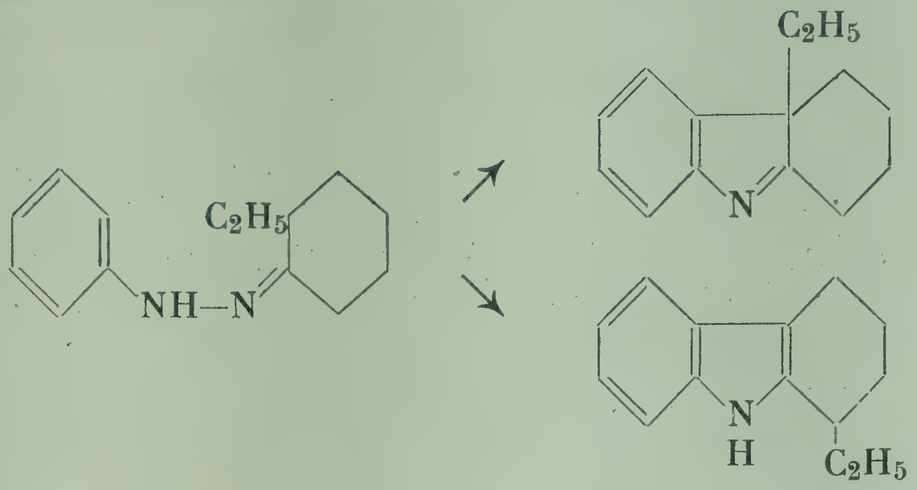


A mixture of N,N′-bis-(1-chloro-2-naphthyl)-α-cyanoformamidine, $AlCl_3$ and NaCl heated in a boiling xylene bath until pasty, then 5 min. longer → 2-(1′-chloro-2′-naphthylimino)-7-chloro-5,6-benzisatin (Y: 75%) heated 20 min. in HCl-acetic acid-water → 7-chloro-5,6-benzisatin (Y: 89%). A. Etienne, Bl. *1949*, 515.

Acetic acid *CH_3COOH*

Fischer indole synthesis

872.



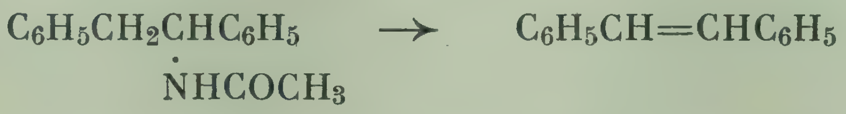
2-Ethylcyclohexanone phenylhydrazone refluxed 0.5 hr. in glacial acetic acid → 11-ethyltetrahydrocarbazolenine (Y: 76%) and 1-ethyltetrahydrocarbazole (Y: 13%).—Whereas H_2SO_4 favors the formation of the neutral 1-subst. tetrahydrocarbazoles, the basic 11-subst. tetrahydrocarbazolenines are the principal products formed when glacial acetic acid is used. F. e. s. K. H. Pausacker, Soc. *1950*, 621.

Phosphorus pentoxide *P_2O_5*

Ethylene derivatives from acylamines

$CHC(NHAc) \rightarrow C{:}C$

873.



$$C_6H_5CH_2\underset{NHCOCH_3}{C}HC_6H_5 \longrightarrow C_6H_5CH{=}CHC_6H_5$$

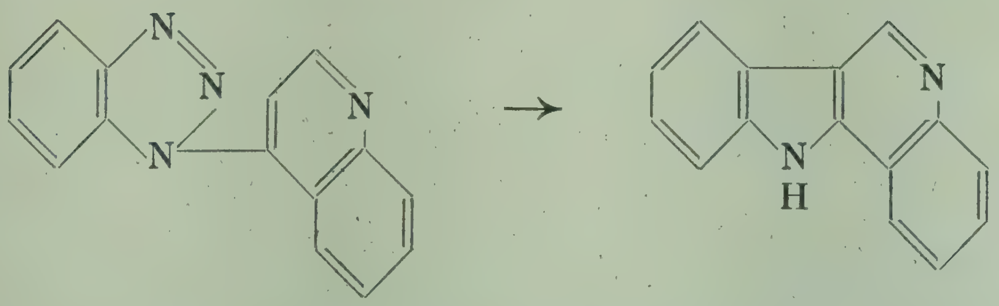
Aceto-1,2-diphenylethylamide and P_2O_5 in xylene refluxed 20 min. → stilbene. Y: 70%. F. e. s. J. W. Cook et al., Soc. *1949*, 1074.

Phosphoric acid *H_3PO_4*

Carbazoles from 1,2,3-triazoles according to Graebe-Ullmann

←

874.



4-(1*H*-Benzotriazol-1-yl)quinoline heated in syrupy H_3PO_4 until the evolution of N_2 ceases → 2,3-benz-γ-carboline. Y: 77%. F. e. s. W. O. Kermack and N. E. Storey, Soc. *1950*, 607.

Hydrochlorides

←

Ethylene derivatives from tert. amines

$CHC(NR_2) \rightarrow C{:}C$

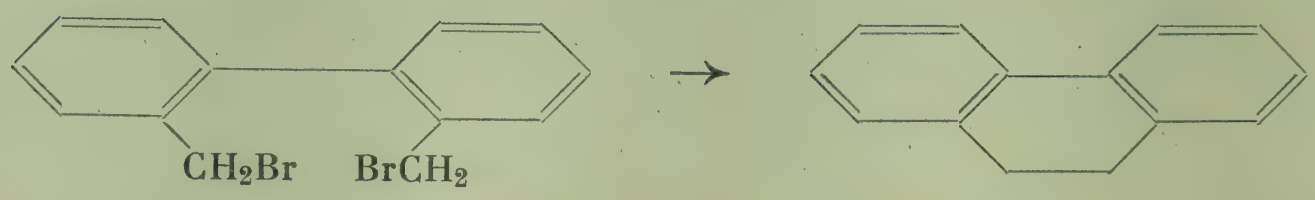
s. *5*, 648; s. a. A. F. Bekhli, Ж. *21*, 86 (1951); C. A. *45*, 7540g

Halogen ↑ **CC ⇑ Hal**

Lithium *Li*

Dihydrophenanthrene ring ○

875.



An ethereal soln. of 2,2′-di(bromomethyl)biphenyl added as rapidly as possible to phenyl-Li from Li and bromobenzene in ether → 9,10-dihydrophenanthrene. Y: 86%. D. M. Hall, M. S. Lesslie, and E. E Turner, Soc. *1950*, 711.

Sodium hydroxide *NaOH*

Cyclopropane ring from halides

s. *3*, 748; cyclopropylketones s. G. W. Cannon, R. C. Ellis, and J. R. Leal, Org. Synth. *31*, 74 (1951)

Potassium hydroxide *KOH*

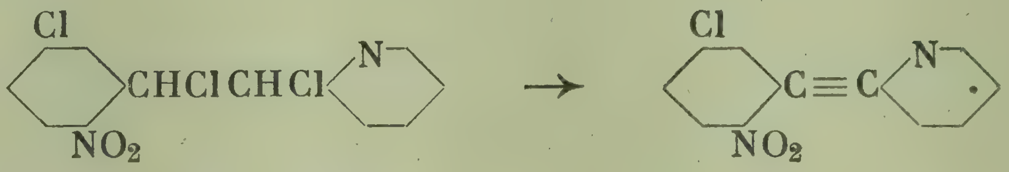
Acetylene derivatives from CH : CHal → C⋮C
***α,β*-ethylenehalides**
Selective dehydrohalogenation

876. $CF_3CH{=}CHJ \rightarrow CF_3C{\equiv}CH$

3,3,3-Trifluoro-1-iodopropene added to a large excess of dried, powdered KOH, and the bath temp. gradually raised from 120° to 150° during 6 hrs → 3,3,3-trifluoropropyne. Y: 68-75%. R. N. Haszeldine, Soc. *1951*, 588.

Acetylene derivatives from CHClCHCl → C⋮C
1,2-dichlorides

877.



KOH in alcohol-water added dropwise during 1 hr. at 95° to 2 gm. 5-chloro-2-nitrostilbazole dichloride in alcohol, and refluxed for a further hr. → 1.36 gm. 5-chloro-2-nitrotolazole. F. e. s. K. Schofield and T. Swain, Soc. *1949*, 2393.

Phenyl lithium *C_6H_5Li*

Acetylene derivatives from CH : CHal → C⋮C
***α,β*-ethylenehalides**

s. *6*, 880

Sodium amide *$NaNH_2$*

Acetylene derivatives from 1,2-dihalides $CHHalCHHal \rightarrow C\vdots C$

Acetyleneamines
Preparation of sodium amide

878. $C_6H_5CHBrCH_2Br \rightarrow C_6H_5C{\equiv}CH$

Finely powdered, dry styrene dibromide added gradually with vigorous stirring to $NaNH_2$ (prepared by adding Na to liq. NH_3 in the presence of $Fe(NO_3)_3$) in liq. NH_3 containing some aniline, and stirring continued for 2 hrs. → phenylacetylene. Y: 45-52%. K. N. Campbell and B. K. Campbell, Org. Synth. *30*, 72 (1950); acetylene amines s. R. F. Parcell and C. B. Pollard, Am. Soc. *72*, 2385 (1950).

Mild dehydrobromination

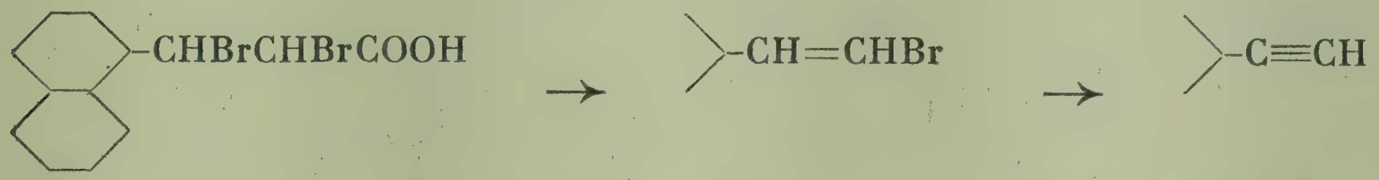
879. $BrCH_2CHBrCH_2CH_2CHBrCH_2Br \rightarrow CH{\equiv}C{\cdot}CH_2CH_2{\cdot}C{\equiv}CH$

1,2,5,6-Tetrabromohexane added dropwise during 2 hrs. to an alcohol-CO_2-cooled, stirred suspension of $NaNH_2$ in liq. NH_3 (prepared from Na with $Fe(NO_3)_3$-catalyst), stirred another 3 hrs., and allowed to stand overnight at room temp., whereby NH_3 evaporates → dipropargyl. Y: 56%. R. A. Raphael and F. Sondheimer, Soc. *1950*, 120; method s. Vaughn, Vogt, and Nieuwland, Am. Soc. *56*, 2120 (1934).

Potassium carbonate *K_2CO_3*

Acetylene derivatives from α,β-dihalogenocarboxylic acids via α,β-ethylenehalides ←

880.



α,β-Dibromo-1-naphthalenepropionic acid treated with cold aq. 10%-K-carbonate → 1-bromo-2-(1-naphthyl)ethylene (Y: 90%) treated with phenyl-Li, then decomposed with water → 1-naphthylacetylene (Y: 90%). D. Bertin, C. r. *229*, 660 (1949).

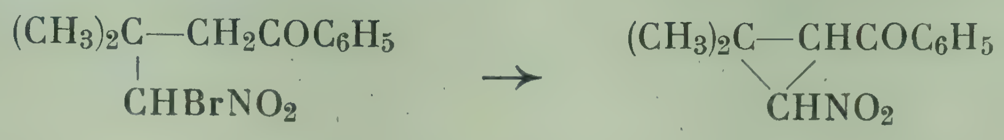
Sodium acetate *CH_3COONa*

Ethylene derivatives from halides $CHCHal \rightarrow C{:}C$

s. *6*, 891

Potassium acetate *CH_3COOK*

Cyclopropane ring from halides ○

881. 

β,β-Dimethyl-γ-bromo-γ-nitrobutyrophenone (prepn. s. 561) dissolved in a soln. of freshly fused K-acetate in dry methanol, allowed to stand at room temp. for 15 hrs., KBr removed, and the filtrate refluxed 13 hrs. until no more KBr separates → 3,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone. Y: 75%. F. e. s. L. I. Smith and V. A. Engelhardt, Am. Soc. *71*, 2671, 2676 (1949).

Alkali iodides ←

Ethylene bromides from tribromides CBrCBr → C:C

s. *4*, 812; with NaI s. Helv. *33*, 2229 (1950)

Sodium iodide *NaI*

Ethylene iodides from 1,2,4-tribromides ←

882. $C_6H_5CHBrCHBrCOCH_2Br \rightarrow C_6H_5CH{=}CHCOCH_2J$

A soln. of 4-phenyl-1,3,4-tribromo-2-butanone in acetone added to a soln. of NaI in acetone, and allowed to stand at room temp. for 3 hrs. → iodomethyl styryl ketone. Y: 90%. P. L. Southwick, L. A. Pursglove, and P. Numerof, Am. Soc. *72*, 1604 (1950).

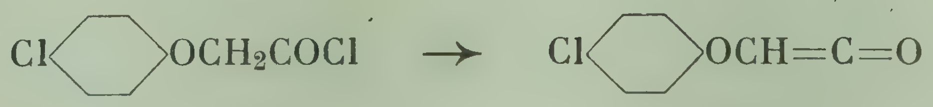
Diethylamine *$(C_2H_5)_2NH$*

Enamines from 1,2-dibromides CHBrCHBr → CH:CN<

s. *6*, 454

Triethylamine *$(C_2H_5)_3N$*

Ketenes from carboxylic acid chlorides CHCOCl → C:C:O

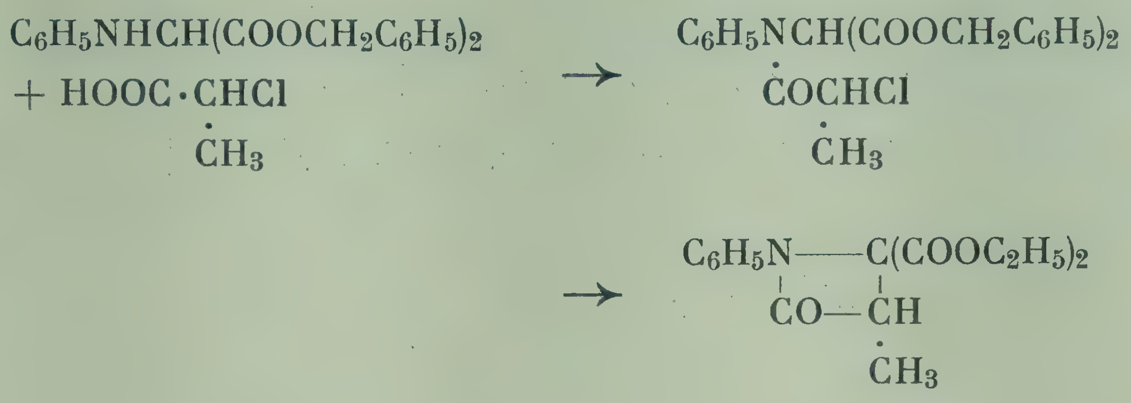
883. 

4-Chlorophenoxyacetyl chloride allowed to react with a small excess of triethylamine → 4-chlorophenoxyketene (startg. m. f. 365). Y: 77.5%. F. e. s. C. M. Hill, G. W. Senter, and M. E. Hill, Am. Soc. *72*, 2286 (1950).

Azetidinones
Subst. carboxylic acid amides from carboxylic acids

○

884.



$$C_6H_5NHCH(COOCH_2C_6H_5)_2 + HOOC\cdot\underset{CH_3}{\dot{C}HCl} \rightarrow \begin{array}{l}C_6H_5NCH(COOCH_2C_6H_5)_2\\ \quad\dot{C}OCHCl\\ \qquad\dot{C}H_3\end{array} \rightarrow \begin{array}{l}C_6H_5N\text{——}C(COOC_2H_5)_2\\ \quad\;|\qquad\quad\;|\\ \quad CO\text{—}CH\\ \qquad\quad\;\dot{C}H_3\end{array}$$

A soln. of dibenzyl anilinomalonate, α-chloropropionic acid, and PCl_3 in benzene refluxed 2 hrs. → dibenzyl N-(α-chloropropionyl)-anilinomalonate (Y: 86.3%) and triethylamine in benzene kept at 50 to 60° overnight → 1-phenyl-3-methyl-4,4-dicarbobenzyloxy-2-azetidinone (Y: 97.6%). F. e. s. J. C. Sheehan and A. K. Bose, Am. Soc. *73,* 1761 (1951); *72,* 5158 (1950).

Quinoline ←

Ethylene derivatives from halides

CHCHal → C:C

s. *6,* 840

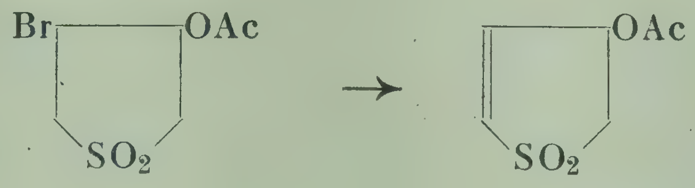
Calcium carbonate *$CaCO_3$*

885. $(ClCH_2CH_2)_2SO_2 \rightarrow (CH_2{=}CH)_2SO_2$

100 gm. 2,2′-dichlorodiethyl sulfone, precipitated $CaCO_3$, and water heated with stirring at 85-90° for 4 hrs. → divinyl sulfone. Y: 79-85%. A. H. Ford-Moore, R. A. Peters, and R. W. Wakelin, Soc. *1949,* 1754.

Barium carbonate *$BaCO_3$*

886.

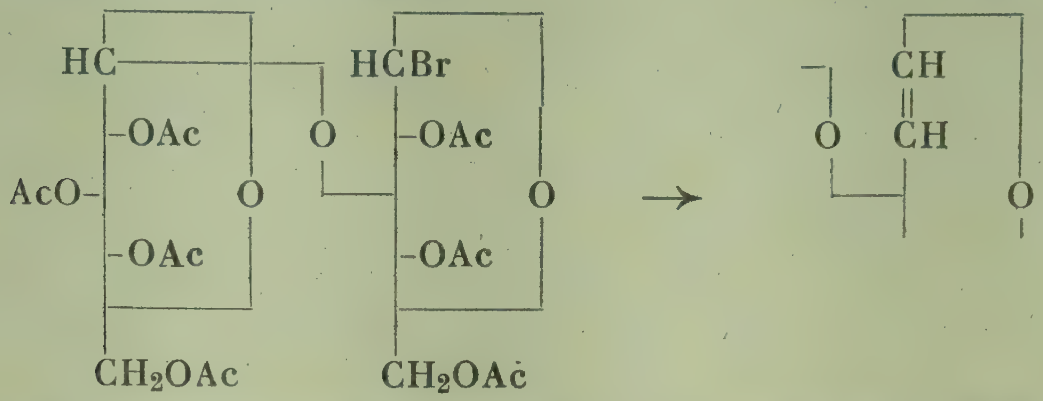


Ethylenesulfones. 3-Bromo-4-acetoxythiacyclopentane, 1,1-dioxide heated with aq. $BaCO_3$ at 85° for 2 hrs. → 4-acetoxythiacyclopent-2-ene 1,1-dioxide. Y: 90%. O. E. van Lohuizen and H. J. Backer, R. *68,* 1137 (1949).

Zinc *Zn*

Glycals from acetobromosugars CBrC(OAc) → C:C

887.



Acetobromoglucosido-3-glucose shaken 2 hrs. with Zn dust in 60%-acetic acid → hexaacetylglucosido-3-glucal (startg. m. f. 282). Y: 80%. A. M. Gakhokidze, Ж. *19,* 2100 (1949); C. A. *44,* 3913f.

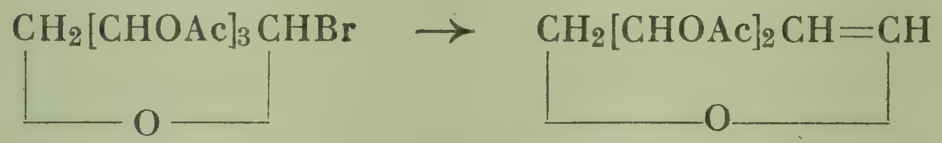
Ethylene derivatives from 1,2-dibromides CBrCBr → C:C

protection of a carbon double bond s. *6,* 280; selective dehalogenation s. A. L. Henne and M. Nager, Am. Soc. *73,* 1042 (1951)

Zinc/hexachloroplatinic acid *Zn/H₂PtCl₆*

Glycals from acetobromosugars CBrC(OAc) → C:C

888.



$$CH_2[CHOAc]_3CHBr \rightarrow CH_2[CHOAc]_2CH{=}CH$$

A soln. of pure β-acetobromo-L-arabinose in glacial acetic acid added at —10° during 10 min. to a stirred mixture of Zn-dust and 50%-acetic acid containing a few drops of chloroplatinic acid soln., which is further added dropwise at intervals of 30 min. to maintain a vigorous reaction, stirring continued for 3 hrs., and kept overnight at 0° → 3,4-diacetyl-L-arabinal. Y: 65%. R. E. Deriaz et al., Soc. *1949,* 1879.

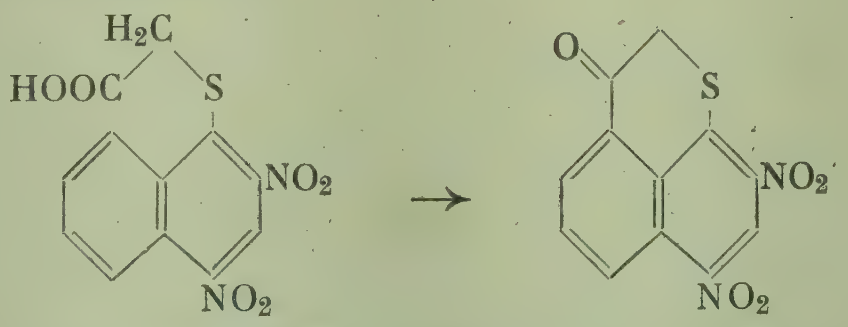
Aluminum chloride *AlCl₃*

Cyclic ketones from carboxylic acid chlorides ○

s. *6,* 861

Naphtho[1.8-bc]thiapyrans

889.



PCl_5 added to a suspension of (2,4-dinitro-1-naphthylmercapto)acetic acid (prepn. s. 647) in CS_2, refluxed until dissolved, cooled to room temp., an ethereal soln. of $AlCl_3$ added, and refluxed for 2 hrs. with frequent shaking → 2,4-dinitronaphtho-1,8-thioindoxyl. Y: 90%.—Other dehydrating agents, e.g. H_2SO_4 and P_2O_5, do not give good results. Solvents other than CS_2 gave poorer yields. G. Leandri, G. *79,* 50 (1949).

Stannic chloride *$SnCl_4$*

Cyclic ketones from carboxylic acids

s. *1,* 778-80; *2,* 808; *4,* 841; s. a. R. C. Gilmore, Jr., and W. J. Horton, Am. Soc. *72,* 733 (1950); D. L. Turner et al., Am. Soc. *72,* 5654 (1950)

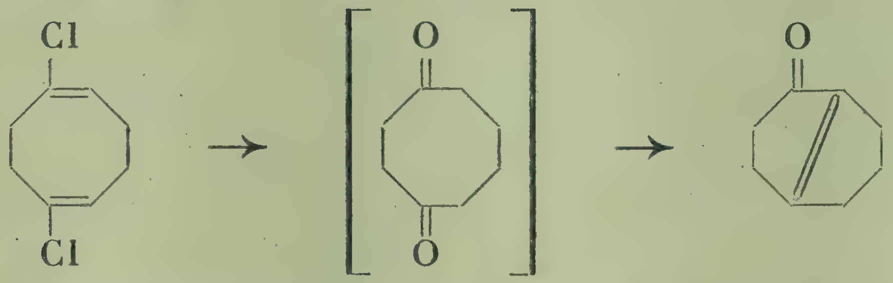
Sulfuric acid *H_2SO_4*

Isocyclics from γ-chlorocrotyl compounds

s. *5,* 654; s. a. M. O. Melikyan and G. T. Tatevosyan, Ж. *21,* 696; C. A. *45,* 9489c

Bicyclo[3.3.0]octane ring from cyclooctane ring ←

90.



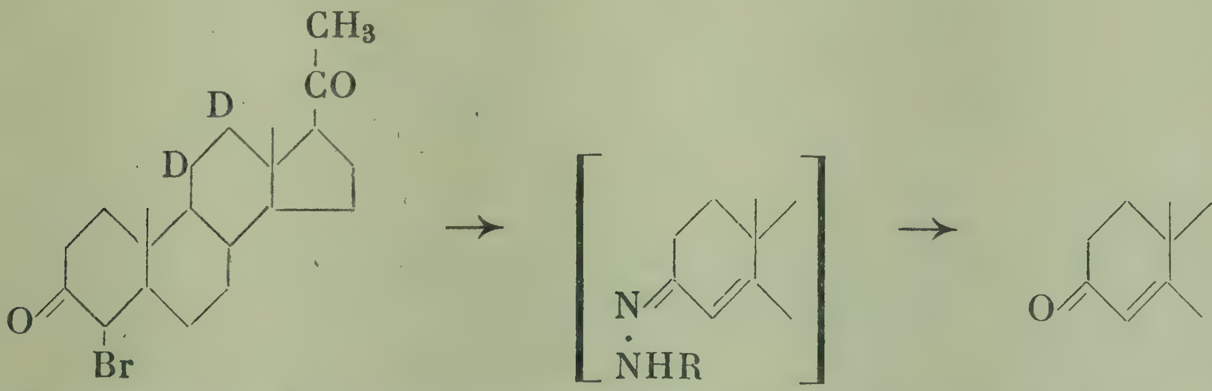
1,6-Dichloro-1,5-cyclooctadiene added dropwise with stirring during 25 min. to ice-cooled concd. H_2SO_4, stirring continued at room temp. for 5 min. and at 70° for 30 min., whereby the HCl evolved is swept from the flask with N_2 → bicyclo[3.3.0]-1(5)-octen-2-one. Y: 70-77%. A. C. Cope and W. R. Schmitz, Am. Soc. *72,* 3056 (1950).

Via intermediates *v.i.*

α,β-Ethylene ketones from α-bromoketones via α,β-ethylenehydrazones Mattox-Kendall reaction CHCHal → C:C

s. *4,* 852; s. a. J. Biol. Chem. *188,* 287 (1951)

91.



Modified procedure. Deutero compounds. Pure 4-bromo-11,12-d_2-pregnane-3,20-dione dissolved in glacial acetic acid at 60°, Na-acetate, followed by 2,4-dinitrophenylhydrazine, added, dissolved under a N_2-stream, kept at 60° for 20 min., during which the mono-2,4-dinitrophenylhydrazone crystallizes, chloroform, Na-acetate, pyruvic acid, and water added, and refluxed 3 hrs. at ca. 70° under a N_2-stream, with repeated additions of pyruvic acid and water until the color changes from red to yellow → 11,12-d_2-progesterone. Y: 80%.—The cleavage is performed without addition of HBr. F. e., also procedure via semicarbazones, s. B. A. Koechlin, T. H. Kritchevsky, and T. F. Gallagher, J. Biol. Chem. *184*, 393 (1950).

Remaining elements ↑ CC ⇑ Rem

Without additional reagents *w.a.r.*

Photoreactions of organo mercury compounds ←

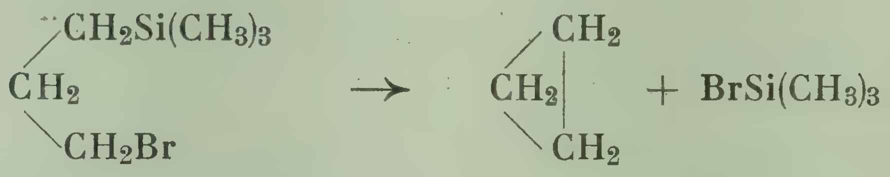
892. $$(C_6H_5CH_2)_2Hg \rightarrow (C_6H_5CH_2)_2$$

Dibenzyl-Hg irradiated in methanol for 50 hrs. → bibenzyl. Y: 80%. F. e. s. G. Razuvaev et al., Ж. *19*, 1487, 1483 (1949), *20*, 175, 181 (1950); C. A. *44*, 3450h, 5832h, 5833b.

Aluminum chloride *$AlCl_3$*

Cyclopropanes from 1,3-halogenosilanes ○
γ-Elimination

893.



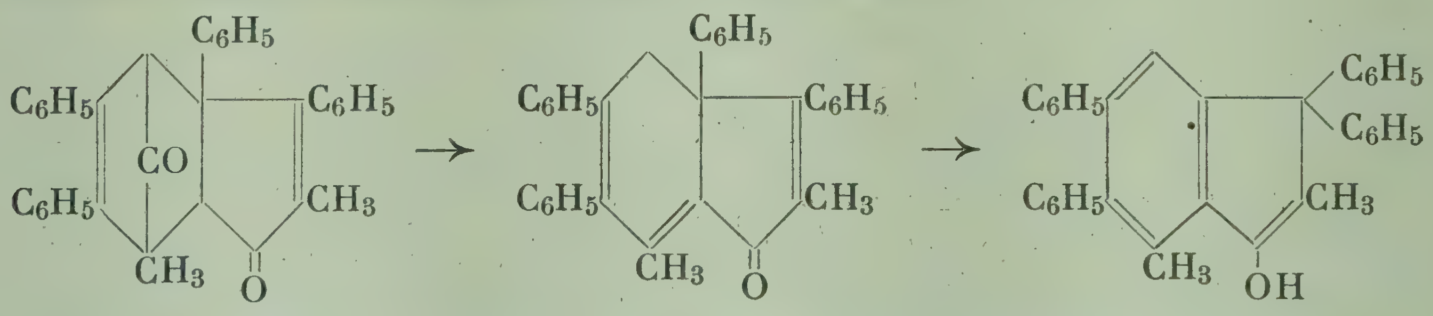
A few crystals of $AlCl_3$ added to γ-bromopropyltrimethylsilane, and warmed to 70° after most of the reaction has taken place → cyclopropane (Y: 92%) and trimethylbromosilane (Y: 82%). L. H. Sommer, R. E. VanStrien, and F. C. Whitmore, Am. Soc. *71*, 3056 (1949).

Carbon ↑ CC ⇑ C

Without additional reagents *w.a.r.*

Benzene ring from endocarbonyl compounds ←

894.



4,7-Endocarbonyl-3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4,7,7a-tetrahydroindenone heated at 240°

for a maximum of 10 min. until the evolution of gas ceased → 3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4-dihydroindenone. Y: 85%.

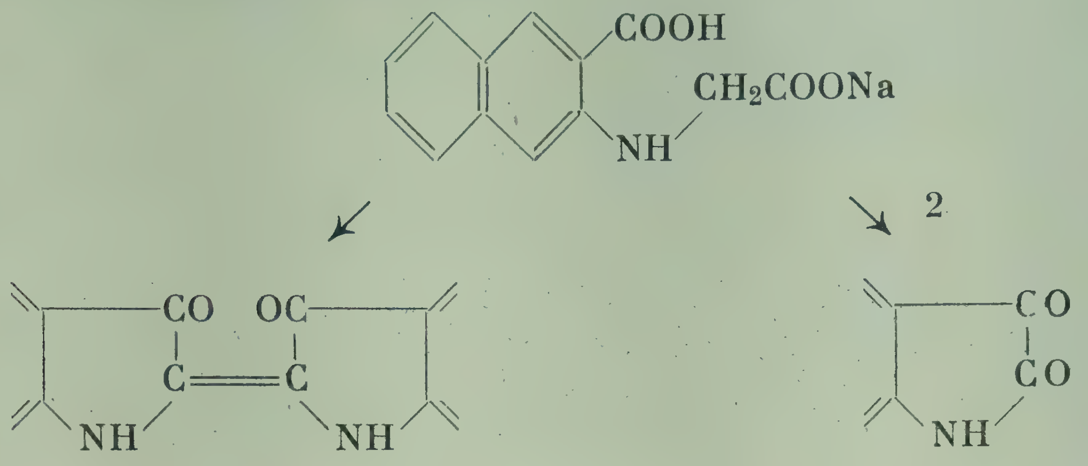
for 3 hrs. → 1,1,5,6-tetraphenyl-2,4-dimethyl-3-hydroxyindene. 7.8 gm. from 10 gm.

C. F. H. Allen and J. A. VanAllan, J. Org. Chem. *14*, 1051 (1949).

Sodium amide/potassium hydroxide *$NaNH_2/KOH$*

Isatins and indigo compounds ○

895.



Na (3-carboxy-2-naphthylamino)acetate added to a mixture of fused KOH and $NaNH_2$

in a porcelain crucible at 200°, heated 15 min. at 210°, dissolved in ice-water, and air passed through → 5,6,5′,6′-dibenzindigo. Y: 60%.

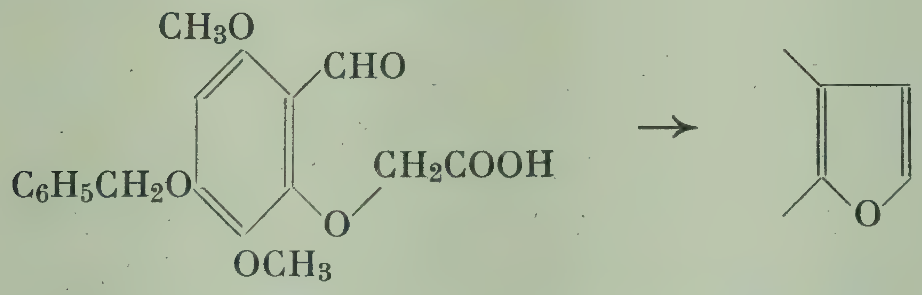
in a copper crucible, kept at 190 to 200° for 15 min., dissolved cautiously in ice-water with exclusion of air, warmed to 80°, and treated dropwise with aq. NH_4-persulfate → 5,6-benzisatin. Y: 85%.

W. Dethloff and K. Schreiber, Chem. B. *83,* 157 (1950).

Sodium acetate *CH_3COONa*

Benzofurans with simultaneous decarboxylation

896.

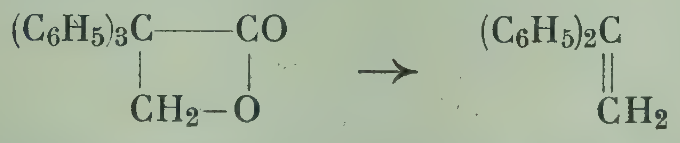


9.7 gm. 5-benzyloxy-3,6-dimethoxy-2-formylphenoxyacetic acid and anhydrous Na-acetate dissolved in acetic anhydride, then refluxed 1 hr. → 6.7 gm. 6-benzyloxy-4,7-dimethoxycoumarone. R. A. Baxter, G. R. Ramage, and J. A. Timson, Soc. *1949,* S30; f. e. s. A. Robertson et al., Soc. *1948,* 2254; *1950,* 2381.

Sodium iodide *NaI*

Ethylene derivatives from lactones ↻

897.



$$\begin{array}{ccc}(C_6H_5)_3C & — & CO\\ | & & |\\ CH_2 & — & O\end{array} \longrightarrow \begin{array}{c}(C_6H_5)_2C\\ \|\\ CH_2\end{array}$$

A soln. of α,α-diphenyl-β-propiolactone in 95% ethanol treated with aq. NaI, and kept at 40° for 112 hrs. → crude 1,1-diphenylethylene. Y: 86%. H. E. Zaugg, Am. Soc. *72,* 2998 (1950).

Ammonia and alkali hydroxide ←

α-Halogen-α,β-ethylenecarboxylic acid esters and acids from β-halogeno-α-keto-γ-lactones C

s. *4*, 855; cf. A. ch. *6*, 247, 322 (1951)

Cuprous cyanide *CuCN*

Acylcyanides and ethylene derivatives from carboxylic acid halides ←

898. $(C_4H_9)_3C\cdot COCl \rightarrow (C_4H_9)_2C{=}CHCH_2CH_2CH_3$

$(CH_3)_3C\cdot COCl \rightarrow (CH_3)_3C\cdot COCN$

A mixture of tributylacetyl chloride and dry CuCn refluxed 8 hrs. by means of a metal bath at 220-240° → 5-butyl-4-nonene. Y: 81%.—Trimethylacetyl chloride and CuCN refluxed 20 hrs. → trimethylacetyl cyanide. Y: 87%. N. Sperber and R. Fricano, Am. Soc. *72*, 2792 (1950).

Aluminum chloride *AlCl$_3$*

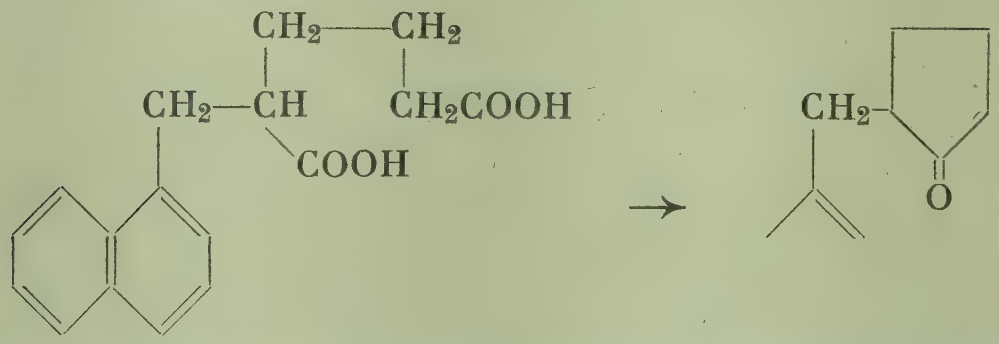
Cyclic aminoketones from N-carboxyaminocarboxylic acid anhydrides ←

s. *6*, 829

Acetic anhydride *(CH$_3$CO)$_2$O*

Cyclic ketones from dicarboxylic acids according to Blanc ○

899.



A soln. of α-(1′-naphthylmethyl) adipic acid in acetic anhydride distilled slowly, after distillation of the acetic anhydride the apparatus filled with N_2, the temp. raised to 300° in the course of 5 min., then the pressure lowered to 30 mm. in order to complete the distillation → 2-(1′-naphthylmethyl)cyclopentanone. Y: 71%. F. e. s. W.E. Bachmann and N. C. Deno, Am. Soc. *71*, 3540 (1949); s. a. P. Pfeiffer and E. Enders, B. *84*, 247 (1951).

Hydrogen peroxide *H$_2$O$_2$*

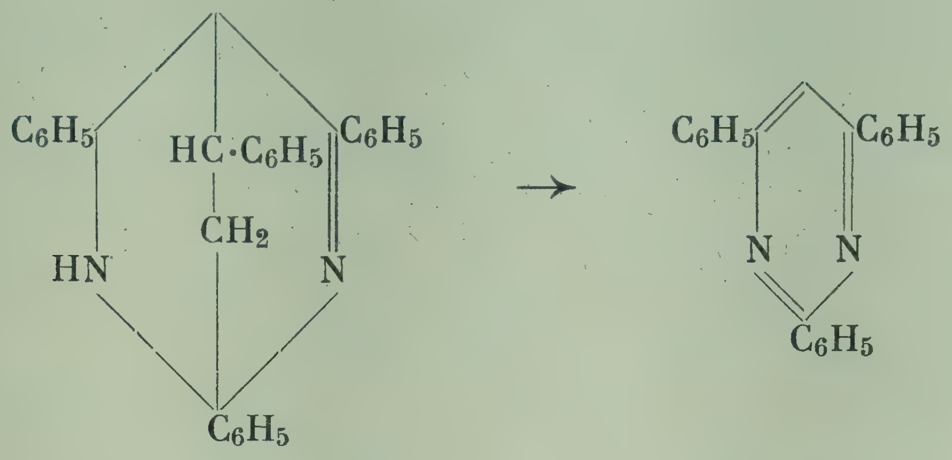
Carboxylic acids from α-ketocarboxylic acids COCOOH → COOH

s. *6*, 747

Sulfur *S*

Aromatization ←

00.

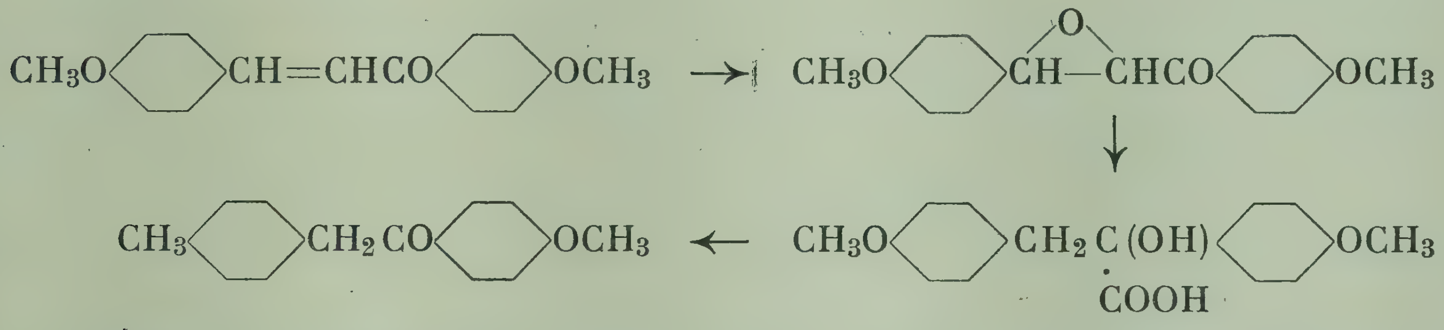


A mixture of 2,4,6-triphenyl-2,5-endo-(2′-phenylethylene)-2-3,4,5-tetrahydropyrimidine and S heated 8 hrs. at 180-190°/8 mm. → 2,4,6-triphenylpyrimidine. Y: 88%. F. e. s. D. E. Piper and G. F. Wright, Am. Soc. *72*, 1669 (1950).

Via intermediates *v.i.*

Desoxybenzoins from chalcones via α,β-oxidoketones and α-hydroxycarboxylic acids ←

01.



4 *N* NaOH and 28%-H_2O_2 added at 40° to a soln. of anisyl p-methoxystyryl ketone in ethanol-acetone, and kept an additional 40 min. at 40° → p-anisyl α,β-epoxy-p-anisylethyl ketone (Y: 92%) refluxed 1.5 hrs. with aq.-alc. NaOH → p-anisyl p-methoxybenzylglycolic acid (Y: 90%), a thick paste of which with glacial acetic acid treated with red Pb-oxide in small portions below 65-70°, at the end of the reaction a few drops of glycerol in water added to destroy any excess Pb-tetraacetate → desoxyanisoin (Y: 98%). E. Rohrmann, R. G. Jones, and H. A. Shonle, Am. Soc. *66*, 1856 (1944); f. e. s. E. R. Bockstahler and D. L. Wright, Am. Soc. *71*, 3760 (1949); E. J. Collins and O. K. Neville, Am. Soc. *73*, 2471 (1951).

2-Step Hooker oxidation ←
Degradation with loss of 1 C-atom

s. *5*, 660; s. a. G. Fawaz and L. F. Fieser, Am. Soc. *72*, 996 (1950); M. Paulshok and C. M. Moser, Am. Soc. *72*, 5073 (1950)

Formation of Electron Pair on Nitrogen

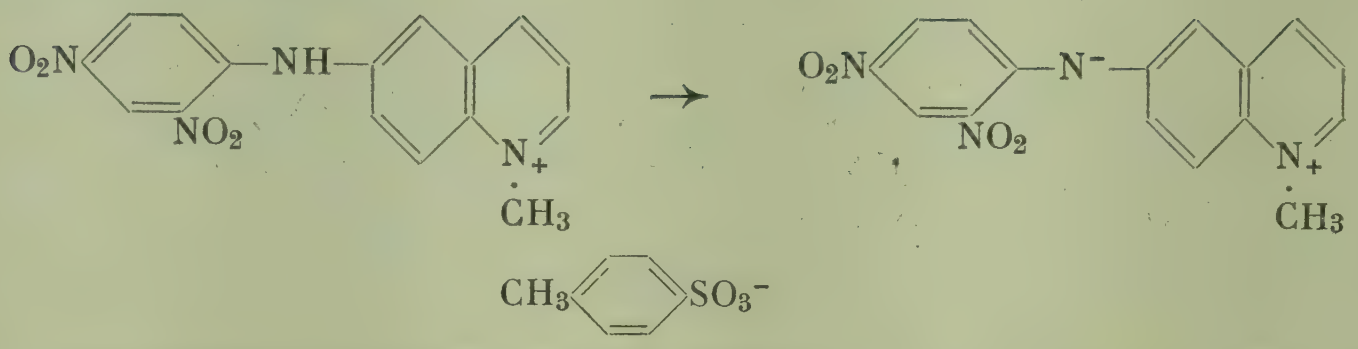
Elimination

Hydrogen ↑ **ElN ⇑ H**

Sodium hydroxide *NaOH*

Betaine azeniates ←

902.

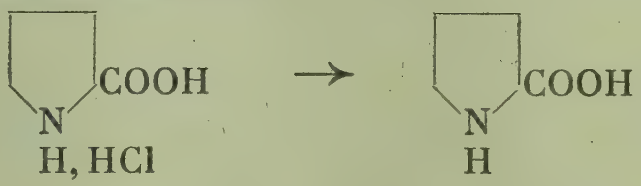


Aq.-alc. NaOH added dropwise at 50-60° to an aq.-alc. soln. of 6-(2,4-dinitroanilino)quinoline metho-p-toluenesulfonate → 6-(2,4-dinitroanilino)-1-methylquinoline betain azeniate. Y: almost 100%. F. e. s. A. M. Simonov, Ж. *20*, 320, 1802 (1950); C. A. *44*, 6863a; *45*, 2460i.

Alkylamines ←

Bases from their hydrochlorides ←

903.



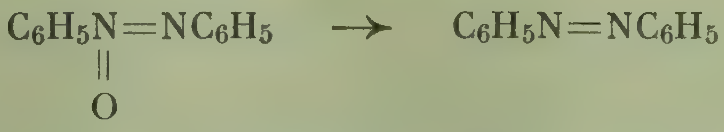
Triethylamine dropped slowly with good stirring into a suspension of proline hydrochloride in dry chloroform, and stirring continued for 1-2 hrs. → DL-proline. Y: 78.5%.—The use of Amberlite resin is less satisfactory. N. F. Albertson and J. L. Fillman, Am. Soc. *71*, 2818 (1949); with diethylamine s. F. E. King and D. A. A. Kidd, Soc. *1949*, 3315.

Oxygen ↑ **ElN ⇑ O**

Carbon oxide *CO*

High pressure reductions with carbon monoxide ←
Azo compounds from azoxy compounds

904.



$$C_6H_5\underset{\underset{O}{\|}}{N}{=}NC_6H_5 \rightarrow C_6H_5N{=}NC_6H_5$$

Nitro-, nitroso-, and azoxy-benzene are reduced to azobenzene, N-phenylhydroxylamine to aniline, and N-phenylbenzaldoxime to benzylideneaniline at 150-250° and 3000 atm. CO-pressure without catalyst. In the presence of Raney-Co, certain α-phenylalcohols are reduced to the corresponding hydrocarbons. Phenols, ethers, esters, amides, ketones, and purely aliphatic alcohols are not reduced by anhydrous CO.—E: 15 gm. azoxybenzene treated with CO at 200° and 3000 atm. for 20 hrs. → 13 gm. azobenzene. F. e. s. G. D. Buckley and N. H. Ray, Soc. *1949,* 1154.

Iron *Fe*

Amines from N-oxides, simultaneously amines from nitro compounds ←

s. *6,* 389

Formation of Electron Pair on Sulfur

Elimination

Oxygen $\uparrow$ ElS $\Uparrow$ O

Lithium aluminum hydride *$LiAlH_4$*

Sym. disulfides from thiosulfonic acid esters $2\,R{\cdot}SO_2SR \rightarrow R{\cdot}SS{\cdot}R$

s. *6,* 47

Formation of Electron Pair on Remaining Elements

Elimination

Oxygen $\uparrow$ ElRem $\Uparrow$ O

Sulfur dioxide/potassium iodide *SO_2/KI*

Arsenoso compounds from arsonic acids $AsO_3H_2 \rightarrow AsO$

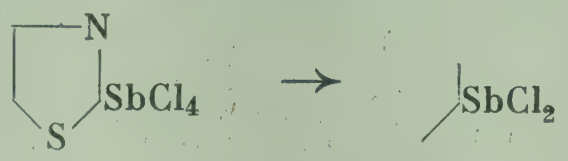
s. *3,* 763; s. a. F. E. Ray and R. J. Garascia, J. Org. Chem. *15,* 1233 (1950)

Halogen ↑ **ElRem ⇑ Hal**

Stannous chloride *SnCl₂*

Antimony(III)- from antimony(V)-compounds ←

905.



Ethanol, satd. with dry HCl, added to an intimate mixture of thiazole-2-stibinic tetrachlodide and $SnCl_2$, and, after 15 min., placed in the cold for crystallization → thiazole-2-stibinous chloride hydrochloride. Y: 80%. F. reactions of organo antimony compounds s. D. B. Meyers and J. W. Jones, J. Am. Pharm. Assoc. *39*, 401 (1950); also reduction with SO_2/HJ s. G. O. Doak and H. H. Jaffé, Am. Soc. *72*, 3025 (1950).

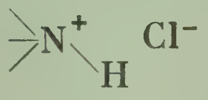
Heteropolar Bond

Uptake

Addition to Nitrogen **Het ⇓ N**

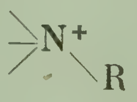
Without additional reagents *w.a.r.*

Hydrochlorides



s. *2*, 829; s. a. M. W. Farlow, Org. Synth. *31*, 62 (1951)

Quaternary ammonium salts



906. $C_6H_5COOCH_2CH_2Cl \rightarrow C_6H_5COOCH_2CH_2J$
$\rightarrow C_6H_5COOCH_2CH_2N^+(CH_3)_3J^-(Cl^-)$

A mixture of anhydrous NaI and methyl ethyl ketone heated 1 hr. on a steam bath with occasional shaking, 2-chloroethyl benzoate added, and heating continued for 22-24 hrs. with occasional shaking → 2-iodoethyl benzoate (Y: 78-81%) allowed to stand with trimethylamine in acetone for 24 hrs. in a closed flask → benzoylcholine iodide (Y: 85 to 90%) added with stirring over a period of 1 hr. at 50-60° to an aq. suspension of AgCl, and stirring continued for a further 30 min. → benzoylcholine chloride (Y: 82-87%). A. H. Ford-Moore, Org. Synth. *30*, 10 (1950).

s. a. H. M. Wuest and E. H. Sakal, Am. Soc. *73*, 1210 (1951)

from dibromides

907. When alkylene dibromides are added to heterocyclic bases, bis-salts are formed in most cases. With glycerol-α,γ-bromohydrin and sterically hindered bases, mono-salts are formed. In several instances, no addition occurred but the alkylene dibromide lost HBr. E. s. J. L. Hartwell and M. A. Pogorelskin, Am. Soc. *72,* 2040 (1950).

Alkyl sulfates

908. In the N-alkylation of tert. amines by unsym. dialkyl sulfates, the smaller alkyl group migrates to the N of the tert. amine. E. s. J. B. Niederl, M. E. McGreal, and W. F. Hart, J. Org. Chem. *14,* 579 (1949).

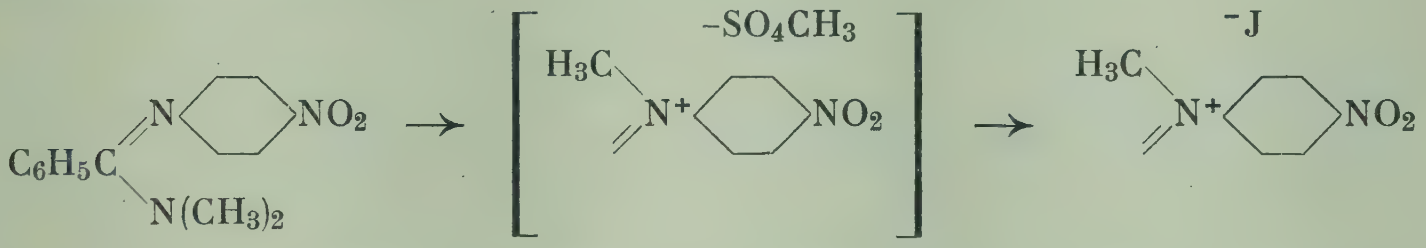
Methosulfates

s. *6,* 820

Via intermediates ***v.i.***

Acridinium salts

909.

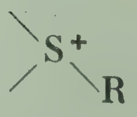


N′-p-Nitrophenyl-N,N-dimethylbenzamidine and acid-free dimethyl sulfate heated at 115-120° until the exothermic reaction ceases, washed with benzene, dissolved in water, and KI added → N′-p-nitrophenyl-N,N,N′-trimethylbenzamidinium iodide. Y: 93%.—The influence of the nitro group was such that no reaction occurred with boiling methyl iodide. E. with methyl iodide, s. C. G. Raison, Soc. *1949,* 3319.

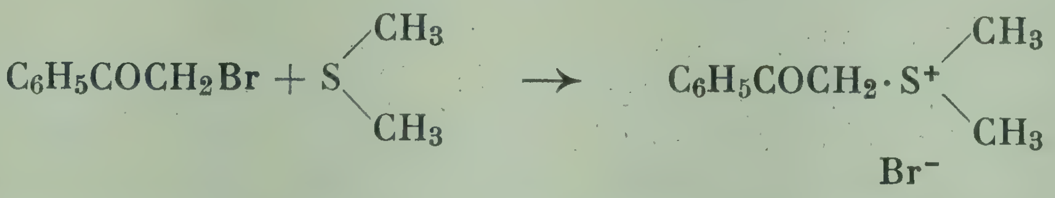
Addition to Sulfur **Het ⇓ S**

Without additional reagents ***w.a.r.***

Sulfonium salts



910.



$$C_6H_5COCH_2Br + S\begin{matrix}CH_3\\CH_3\end{matrix} \rightarrow C_6H_5COCH_2\cdot S^+\begin{matrix}CH_3\\CH_3\end{matrix}\ Br^-$$

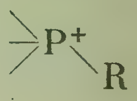
Dimethyl sulfide added to a soln. of ω-bromoacetophenone in acetone-water, and allowed to stand ca. 0.5 hr. → dimethyl phenacyl sulfonium bromide. Y: 85%. F. e. s. H. Böhme and W. Krause, Chem. B. *82*, 426 (1949).

with simultaneous formation of ketals
s. *6*, 212

Addition to Remaining Elements **Het ⇓ Rem**

Without additional reagents *w.a.r.*

Phosphonium salts



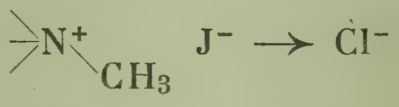
911. $(C_2H_5)_3P + C_{12}H_{25}Br \longrightarrow (C_2H_5)_3P^+C_{12}H_{25}\ \ Br^-$

Triethyl phosphine and dodecyl bromide heated 12 hrs. at 90° in a sealed tube → dodecyltriethylphosphonium bromide. Y: 80%. F. e. s. D. Jerchel and J. Kimmig, B. *83*, 277 (1950); arylphosphonium salts s. K. Kröhnke, B. *83*, 291 (1950).

Exchange **Het ⇅**

Silver chloride *AgCl*

Methochlorides from methiodides
s. *6*, 724, 906



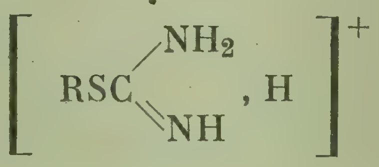
Amberlite ←

Acids from their salts ←

An aq. soln. of Na-inositol-5-phosphate (prepn. s. 14) passed through a column containing moist Amberlite-IR-100AG → inositol-5-phosphoric acid (startg. m. f. 10). Y: 82%. B. M. Iselin, Am. Soc. *71*, 3822 (1949).

Halides *Hal⁻*

Thiouronium salts as used for the characterization of carboxylic acids
s. *1*, 791; s. a. H. M. E. Cardwell, Soc. *1950*, 1207



Index

Cumulative Index, Volumes 1 – 5, see Volume 5, page 503

The subject index lists the names of the methods, types of compounds, reagents, etc. For specific compounds and for authors (when a method is not named after them) the reader may be referred to the indexes of abstract journals. Complex compounds, as those with several functional groups, are referred to under the related simpler compounds, under *special s.* E.g. *aminocarboxylic acids* are found under *carboxylic acids*. Only compounds beginning with letters other than those of the parent or main compounds are listed under this subentry, and entry numbers are omitted because they are specified when the compound is given as a main entry. Methods of synthesis for a given substance are indexed under the name of this substance and the subentry *from*, e.g. carboxylic acids from alcohols, hydrocarbons. Syntheses carried out from a particular starting material are indexed under the starting material and the subentry *startg. m. f.* (starting material for the preparation of . . .), e.g. alcohols, startg. m. f. carboxylic acids, ketones.

Classes of compounds may be designated merely by the functional group that is changed during the reaction. Ring compounds may also refer to the corresponding hydrogenated rings, unless the latter are listed specifically. If that be the case, then, as in several other cases, the *inversion* has been made use of that is customary in the indexes of Chemical Abstracts. Dihydrofurans, e.g., may be found under Furans, dihydro-. All single letters, which are separated from the name by a hyphen, are being ignored in regard to alphabetic arrangement, e.g., 'O-Acetyl derivatives' are listed under A.

Register

Generalregister, Band 1—5, siehe Band 5, Seite 503

Im alphabetischen Register finden sich als Schlagworte Methoden, Verbindungsklassen, Reagenzien u. dgl.; Einzelverbindungen und Autoren, soweit nicht eine Methode nach ihnen benannt ist, sind, wie bisher, in den Registern der Referatenblätter zu suchen. Auf kompliziertere Verbindungen, z. B. mit mehreren funktionellen Gruppen, ist

bei den entsprechenden einfacheren Verbindungen unter *special s.* (spezielle siehe) hingewiesen, z. B. bei Carbonsäuren auf Aminocarbonsäuren. Es wird hier jedoch nur auf Verbindungen hingewiesen, die einen anderen Wortanfang haben und deshalb an anderer Stelle im Register stehen. Methoden zur Synthese eines bestimmten Endprodukts findet man beim Schlagwort dieses Endprodukts unter *from* (aus) registriert, z. B. Carbonsäuren aus Alkoholen, Kohlenwasserstoffen. Synthesen, die sich mit einem bestimmten Ausgangsmaterial ausführen lassen, sind bei dem Schlagwort des Ausgangsmaterials unter *startg. m. f.* (Ausgangsmaterial für die Darstellung von ...) zu suchen, z. B. Alkohole, Ausg. f. Ketone, Carbonsäuren.

Die Bezeichnung der Verbindungsklassen kann sich auf funktionelle Gruppen beschränken, die bei der Reaktion verändert werden. Ringbezeichnungen können sich auch auf die entsprechenden hydrierten Ringe beziehen. Sind hydrierte Ringe aber besonders aufgeführt, dann ist bei ihnen, wie auch in einigen anderen Fällen, von der Inversion Gebrauch gemacht worden, wie sie in den Sachregistern der «Chemical Abstracts» üblich ist. Z. B. stehen Dihydrofurane unter Furane, Dihydro-. Griechische Buchstaben und Einzelbuchstaben, die vom eigentlichen Namen durch Bindestrich getrennt sind, werden bei der alphabetischen Anordnung nicht berücksichtigt, z. B. stehen «O-Acetyl-derivate» unter A.

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  alkoxyhalides
  chlorides
  dihalides
  ethylene-halides
  hydroxy-
  nitro-
  oxido-
  poly-
  tri-
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with 1 O-atom
benzofurans
chromones
coumarins
furans
pyrans
xanthenes

with 1 N-atom
acridines
anthrapyridonacridones
anthrapyridones
4-azafluoranthenes
azafluorenes
carbazoles
1H-indeno[2.1-c]pyridines
indoles
isoquinolines
phenanthridines (9-azaphenanthrenes)
pyridines
pyrroles
quinolines

with 1 hetero atom other than O and N
naphtho[1.8-bc]thiapyrans
thianaphthenes (benzothiophenes)
thiophenes

with 2 O-atoms
benzo-1,3-dioxanes
chromono(3′,2′,3,4)coumarins
m-dioxanes
α-pyrono(5′,6′,3,4)coumarins

with 2 N-atoms
2,4-diazafluoranthenes
1,3-diazacycloalkenes
imidazoles (glyoxalines)
imidazo[1.2-a]pyrroles
indazoles
naphthyridines (diazanaphthalenes)
phenazines (5,10-diazaanthracenes)
phthalazines (2,3-diazanaphthalenes)
pyrazines
pyrazoles
pyridazines
9(H)-pyrid[3.4-b]indoles

pyrimidazoles
pyrimidines
pyrrolo[2.1-b]quinazolines
quinazolines (1,3-diazanaphthalenes)
quinoxalines (1,4-diazanaphthalenes)
with 2 hetero atoms other than O and N
1,2-dithioles
with 2 different hetero atoms
benz-3,1-oxazines
benzoxazoles
isoxazoles
1,2-oxazines
1,4-oxazines (morpholines)
oxazoles
thiazoles
with 3 or more hetero atoms
benzothiadiazoles
1,3,4-oxadiazoles
porphyrins
purines
pyrimido 4.5-b pyrazines (1,3,5,8-tetraazanaphthalenes)
1,2,3,4-tetrazines
tetrazoles
1,2,4-thiadiazine 1,1-dioxides
1,2,5-thiadiazines
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thiazolo 3.2-a pyrimidines
thiazolo 5.4-d pyrimidines
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  aminohydroxy compounds
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CC ⇑ O
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Deutscher Schlüssel zum Register (Index)

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Abspaltung	Elimination
Acylessigester	Acylacetic esters
Acylhydrochinonäther	Acylquinol ethers
Acylierung	Acylation
Aether	Ethers
Aethyl-	Ethyl-
Alkoholate	Alkoxides
Alkohole	Alcohols
Alkylidenacetessigester	Alkylideneacetoacetic esters
Alkylierung	Alkylation
Allylumlagerung	Allyl rearrangement
Ameisensäure	Formic acid
Anhydrozucker	Anhydrosugars
Anlagerung	Addition
Arylierung	Arylation
Asparaginsäuren	Aspartic acids
Aufbau	Synthesis
Austausch	Replacement
Benzolringsystem	Benzene ring system
Benzopersäure	Perbenzoic acid
Bernsteinsäure	Succinic acid
Bimsstein	Pumice
Blei	Lead
Bor	Boron
Borsäure	Boric acid
Borsäureanhydrid	Boron trioxide
Brenztraubensäure	Pyruvic acid
Brom	Bromine
Brom-	Bromo-
Bromcyan	Cyanogen bromide
Bromjod	Iodine bromide
Carbäthoxylierung	Carbethoxylation
Carbonsäure-	Carboxylic acid-
Carbonsäuren, verzweigte	Carboxylic acids, branched
Chlor	Clorine
Chlor-	Chloro-
Chloressigsäure	Chloroacetic acid
Chlorjod	Iodine monochloride
Chlorschwefel	Sulfur monochloride
Chrom	Chromium
Chin-	Quin
Cumarin	Coumarin

	siehe unter
Dehydratisierung	Dehydration
Dehydrierung	Dehydrogenation
Diazokupplung	Diazo coupling
Einführung von funktionellen Gruppen	Replacement of hydrogen
Eisen	Iron
Erdalkalien	Earths, alkaline
Erden, seltene	Earths, rare
Fluorwasserstoffsäure	Hydrogen fluoride
Gallensäurederivate	Bile acid derivatives
Glycerine	Glycerols
Halbacetale	Hemiacetals
Halogenide	Halides
Halogenwasserstoff	Hydrogen halide
Harnsäuren	Uric acids
Harnstoff	Urea
Heterocyclen	Heterocyclics
Holzkohle	Charcoal
Hydrierung	Hydrogenation
Hypohalogenite	Hypohalites
Isocyclen	Isocyclics
Isothioharnstoffe	Isothioureas
Jod	Iodine
Jod-	Iodo-
Jodwasserstoffsäure	Hydrogen iodide
Kalium	Potassium
Kern	Nucleus
Kettenverlängerung	Chain lengthening
Kohlehydrate	Carbohydrates
Kohlendioxyd	Carbon dioxide
Kohlensäure	Carbonic acid
Kohlenwasserstoffe	Hydrocarbons
Kunstharz-Base	Resin base
Kupfer	Copper
Kupplung	Coupling
Mangan	Manganese
Molekülverbindungen	Molecular compounds
Natrium	Sodium
Natriumäthylat	Sodium ethoxide
Oxy-	Hydroxy-
Oxydation	Oxidation
Peressigsäure	Peracetic acid
Phosphinsäuren	Phosphonic acids
Polymerisierung	Polymerization

	siehe unter
Quecksilber	Mercury
Razemate	Racemates
Reduktions-Tropfverfahren	Dropping reduction
Ringerweiterung	Ring enlargement
Ringöffnung	Ring opening
Ringschluß	Ring closure
Ringverengung	Ring contraction
Salpetrigsäureester	Nitrous acid esters
Salpetersäure	Nitric acid
Schutz	Protection
Schwefel	Sulfur
Schwefelchloride	Sulfur chlorides
Schwefelwasserstoff	Hydrogen sulfide
Seitenketten	Side chains
Senföle	Isocyanates
Silicium	Silicon
Siliciumdioxyd	Silica
Spaltung	Cleavage
Stellungswechsel	Position shift
Stickstoff	Nitrogen
Stickstoffwasserstoffsäure	Hydrazoic acid
Sulfaminsäuren	Sulfamic acids
Sulfopersäure	Peroxymonosulfuric acid
Thiohalogenide	Sulfenylhalides
Thioharnstoff	Thiourea
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Tschitschibabin	Chichibabin
Tschugaeff	Chugaeff
Umacylierung	Transacylation
Umesterung	Transesterification
Umkehrung	Inversion
Umlagerung	Rearrangement
Unterphosphorigsäure	Hypophosphorous acid
Verbindungen	Compounds
Veresterung	Esterification
Verseifung	Hydrolysis
Wanderung	Migration
Wasserstoffperoxyd	Hydrogen peroxide
Wismutverbindungen	Bismuth compounds
Zinn	Tin
Zuckersäuren	Saccharic acids

Abbreviations - Abkürzungen

abs.	absolute	absolut
alc.	alcoholic	alkoholisch
aq.	aqueous	wäßrig
ar.	aromatic	aromatisch
atm.	atmosphere(s)	Atmosphäre(n)
cf.	compare	vergleiche
concd.	concentrated	konzentriert
d.	density	Dichte
dil.	diluted	verdünnt
et al.	and others	und andere
E.	example	Beispiel
e.g.	for example	zum Beispiel
F. e. s.	Further example(s) see	weitere(s) Beispiel(e) siehe
hr(s).	hour(s)	Stunde(n)
liq.	liquid	flüssig
min.	minutes	Minuten
N	normal	normal
prepn.	preparation	Darstellung
prim.	primary	primär
s.	see	siehe
s. a.	see also	siehe auch
satd.	saturated	gesättigt
sec.	secondary	sekundär
soln.	solution	Lösung
startg. m. f.	starting material for (the preparation of...)	Ausgangsmaterial für die Darstellung von...
subst.	substituted	substituiert
sym.	symmetrical	symmetrisch
temp.	temperature(s)	Temperatur(en)
tert.	tertiary	tertiär
v.i.	via intermediates	über Zwischenprodukte
w.a.r.	without additional reagents	ohne Hilfsstoffe
Y *)	yield	Ausbeute

*) When yields are listed in parentheses, the yields so designated refer to the immediately preceding step of a multi-step reaction.

Bei mehrstufigen Synthesen beziehen sich eingeklammerte Ausbeuteangaben auf die unmittelbar vorhergehende Stufe.

Symbols - *Zeichen*

(on the right half of the page) (auf der rechten Hälfte der Seite)

Electrolysis	↯	Elektrolyse
Ring closure	○	Ringschluß
Ring opening	↻	Ringöffnung
'see title on the left half of the page'	←	«siehe Titel auf der linken Hälfte der Seite»

Journal Abbreviations - *Zeitschriften-Abkürzungen*

A.	Liebig's Annalen der Chemie
A. ch.	Annales de Chimie
Am. Soc.	Journal of the American Chemical Society
Ar.	Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft
Ark. Kemi	Arkiv för Kemi, Mineralogi och Geologi
B.	Chemische Berichte
Bl.	Bulletin de la Société Chimique de France
C. A.	Chemical Abstracts
C. r.	Comptes rendus (Paris)
G.	Gazzetta Chimica Italiana
H.	Hoppe Seyler's Zeitschrift für physiologische Chemie
Helv.	Helvetica Chimica Acta
J. Org. Chem.	Journal of Organic Chemistry
J. pr.	Journal für praktische Chemie
M.	Monatshefte für Chemie
Org. Synth.	Organic Syntheses
R.	Recueil des Travaux Chimiques des Pays-Bas
Ж	Journal of General Chemistry (Russia)
Soc.	Journal of the Chemical Society
Synth. Meth.	Synthetische Methoden der Organischen Chemie

For other journal abbreviations see Beilstein, Handbuch der organischen Chemie or Chemical Abstracts.

Die übrigen Zeitschriften-Abkürzungen siehe Beilsteins Handbuch der organischen Chemie oder Chemical Abstracts

Systematic Survey - Systematische Uebersicht

Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite
HO ⇓ O	1	OS ⇵ S	57	NS ⇵ H	124
HO ⇓ OC	1	OS ⇑ O	58	NS ⇵ Hal	124
HO ⤺ HC	2	ORem ⇓ OC	58	NS ⇑ H	125
HO ⇵ Hal	2	ORem ⇓ Rem	58	NS ⇑ S	125
HO ⇵ S	3	ORem ⇵ H	59	NRem ⇵ O	125
HO ⇵ Rem	4	ORem ⇵ N	59	NRem ⇵ Hal	126
HO ⇵ C	4	ORem ⇵ Hal	59	NRem ⇵ Rem	126
HN ⇓ ON	10	ORem ⇵ S	61	NC ⇓ OC	126
HN ⇓ NN	10	OC ⇓ HC	61	NC ⇓ NC	130
HN ⤺ HO	11	OC ⇓ OC	63	NC ⇓ SC	134
HN ⇵ O	11	OC ⇓ NC	66	NC ⇓ CC	135
HN ⇵ N	14	OC ⇓ SC	67	NC ⤺ HN	138
HN ⇵ S	14	OC ⇓ CC	68	NC ⤺ OC	138
HN ⇵ C	14	OC ⤺ HO	72	NC ⤺ SC	139
HS ⇵ Hal	18	OC ⤺ HC	72	NC ⤺ CC	140
HS ⇵ S	18	OC ⤺ OC	74	NC ⇵ H	141
HS ⇵ C	18	OC ⤺ NC	74	NC ⇵ O	144
HRem ⇵ Hal	20	OC ⤺ CC	75	NC ⇵ N	161
HC ⇓ OC	20	OC ⇵ H	76	NC ⇵ Hal	164
HC ⇓ NC	26	OC ⇵ O	78	NC ⇵ S	173
HC ⇓ SC	29	OC ⇵ N	84	NC ⇵ C	177
HC ⇓ CC	29	OC ⇵ Hal	91	NC ⇑ H	182
HC ⤺ HO	36	OC ⇵ S	98	NC ⇑ O	182
HC ⇵ O	36	OC ⇵ Rem	101	NC ⇑ N	189
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OS ⇓ HO	55	NN ⇵ H	120	HalRem ⇵ H	194
OS ⇓ S	56	NN ⇵ O	122	HalRem ⇵ O	195
OS ⇵ H	56	NN ⇑ H	123	HalRem ⇵ Hal	195
OS ↓ Hal	56	NS ⇓ SC	123	HalRem ⇵ S	196

Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite
HalRem ⇅ C	196	SC ⇅ Hal	231	CC↶SC	265
HalC ⇓ OC	197	SC ⇅ S	236	CC↶CC	266
HalC ⇓ NC	198	SC ⇅ C	237	CC ⇅ H	266
HalC ⇓ CC	199	SC ⇑ H	238	CC ⇅ O	267
HalC↶HC	201	SC ⇑ O	238	CC ⇅ N	290
HalC ⇅ H	201	SC ⇑ N	239	CC ⇅ Hal	294
HalC ⇅ O	207	RemRem ⇅ S	239	CC ⇅ S	306
HalC ⇅ N	212	RemC ⇓ OC	239	CC ⇅ C	306
HalC ⇅ Hal	213	RemC ⇓ CC	240	CC ⇑ H	310
HalC ⇅ C	214	RemC ⇅ H	240	CC ⇑ O	313
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SS ⇅ O	215	RemC ⇅ N	241	CC ⇑ Hal	328
SS ⇅ Hal	215	RemC ⇅ Hal	241	CC ⇑ Rem	334
SS ⇅ S	216	RemC ⇅ Rem	243	CC ⇑ C	334
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SC ⇓ OS	217	CC ⇓ HC	244	ElN ⇑ O	338
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LiH, NaH
Na,Hg
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Aq. alkali hydroxide
NaOH, KOH
Alkali in water a. alcohol
NaOH/alcohols
KOH/alcohols
Alkali alkoxide
Na/alcohol, NaOR
K/alcohol, KOR, K-tert-butoxide
C_6H_5Li
$(C_6H_5)_3C\cdot Na$
$LiNH_2$, Li-methylanilide
Na/liq. NH_3, $NaNH_2$, Na-anilide
Alkali in pyridine
Na_2O_2
Na_2CO_3, $NaHCO_3$, K_2CO_3, $KHCO_3$
HCOONa
CH_3COONa, CH_3COOK
Na-citrate
NaCN, KCN
KSCN
$NaNO_2$
KNO_3
KH_2PO_4
K-xanthate
Na_2S, Na_2S_2, Na_2S_x, NaHS
Na_2Se_x
KHS
$Na_2S_2O_3$
Na_2SO_3, $NaHSO_3$
NaF, KF, KHF_2
Alkali iodides
NaI, KI
Alkali salts
Alkaloid-alkali salts
Na^+, Sodium compound, K^+
NH_3
Organic bases
Resin base
Triton B, BTAB
Alkylamines
Methylamine, n-Butylamine
Benzylamine
Diethylamine,
Aliphat. tert. amines
Triethylamine
Piperidine, Morpholine
N-Methylmorpholine
Aniline
Dialkylaniline
Dimethylaniline, Diethylaniline
Pyridine, Lutidine, Collidine, Quinoline
Cu, Ag, Ag-Cu, Cu,Mg
Copper oxide, Cu_2O, CuO
Ag_2O
Ag_2CO_3
CH_3COOAg
Cupric carbonate, basic
$(CH_3COO)_2Cu$
Fehling solution
Copper borate
CuCN
CuSCN
Cu(I,II) sulfite
CuCl, CuBr/Mg, CuI/Mg, Cu_2Cl
Cu^+, Cu^{++}
AgCN
AgN_3
$AgNO_2$
$AgNO_3$
AgF-Cu
C_6H_5COOAg
Ag^+
CaO, BaO, BaO-SiO_2
$Ca(OH)_2$, $Ba(OH)_2$
$Ba(OR)_2$
$CaCO_3$, $BaCO_3$
$(CH_3COO)_2Ba$
$CaSO_4$
$CaCl_2$, $BaCl_2$-C
Mg, Mg,Hg, Mg/MgI_2
Zn, Zn,Cu, Zn,Hg
Cd, Hg
HgO, MgO
$Mg(OH)_2$
$Mg(OR)_2$
CH_3MgI
C_6H_5MgBr
Zinc alkyls, Zinc alkyl halides
$(CH_3\ COO)_2Hg$
$Zn(CN)_2$, $Hg(CN)_2$
$Hg(ONC)_2$ (fulminate)
$Mg(NO_3)_2$
$BeSO_4$, $MgSO_4$, $HgSO_4$
$MgBr_2$
$ZnCl_2$, $ZnCl_2\cdot 2NH_3$
$HgCl/CdCO_3$
$HgCl_2$, $HgBr_2$
Mg^{++}, Ca^{++}, Zn^{++}, Hg^{++}
Al, Al,Cu, Al,Hg
$NaBH_4$, $LiAlH_4$
B_2O_3, HBO_2
Al_2O_3
$Al(OR)_3$
Al isopropoxide, Al tert-butoxide
Al phenoxide
Al silicate
Pumice
Glass powder
$AlPO_4$/water glass
BF_3
HBF_4
$AlCl_3$, $AlBr_3$
Al^{+++}
Ce and rare earths
C
Alkoxides
CH_3OH

Hydroquinone
Oxo compounds
Benzophenone
Quinone
Ketene
D-Lactose hydrate
Pyruvic acid
$(NH_4)_2CO_3$
$HCOONH_4$, CH_3COONH_4
NH_4SCN
Salts of organic bases
Acetates of organic bases
Piperidinium acetate
Diazomethane
Hexamethylenetetramine
$HCONH_2$
$HCON(CH_3)_2$
$CO(NH_2)_2$
Phenyl isocyanate
Emulsin
Hog kidney enzyme
Chymotrypsin
Papain
Acetobacter suboxydans
Nitrosobenzene
Nitrosodimethylaniline
Isonitrosocyanoacetic ester
Isopropane nitronate
Nitrobenzene
$(CH_3CO)_2O$
Ascaridole
Acyl peroxides
Acetyl-, Benzoyl peroxide
Phenol, Pyrogallol
$HCOOH$, CH_3COOH,
CH_3CH_2COOH
Thioacetic acid
$ClCH_2COOH$, CCl_3COOH
$(COOH)_2$, $CH_2(COOH)_2$, Phthalic acid
CO_3^{--}
Peroxy acids
$HCOO_2H$, CH_3COO_2H
$C_6H_5COO_2H$, Perphthalic acid
Thioureas
Thiocyanates
Dimethyl sulfate
Sulfonamides
Amyl disulfide
Methyl tetrasulfide
CH_3I
Polyhalogenoalkanes
CCl_3H, CCl_3Br
Benzotrichloride
Iodobenzene dichloride
BrCN
Bromoacetamide
Chlorourea
Bromosuccinimide, Bromophthalimide
Chloramin-T
Chloranil
$COCl_2$
CH_3COCl, $(COCl)_2$
C_6H_5COCl, C_6H_5COBr
$(CH_3)_2CHCHBrCOBr$
SiO_2, SiO_2-Al_2O_3
$TiO_2/HCOOH$
$SiCl_4$
Sn
$SnCl_2$, $SnCl_4$
PbR_4
PbO, Pb_3O_4, PbO_2
$Pb(OH)_2$
$(CH_3COO)_2Pb$
$(CH_3COO)_4Pb$
Pb^{++}
ThO_2
Dicyanodiamide
Phenylhydrazine
$H_2N{\cdot}NH_2$
N_3^-, HN_3
NH_2OH
Nitrogen oxides
N_2O_3, N_2O_4, N_2O_5
NH_4NO_3
Alkyl nitrite
Butyl-, Amyl nitrite
NO_2^-
NOCl, NOBr
HNO_3
P
Phosphorus compounds
PH_4I
Phosphazo compounds
P_2O_5
$H_2PO_2^-$
H_3PO_2
Quinoline phosphate
H_3PO_4
P_2S_3, P_2S_5
$PHal_3$, PCl_3, PBr_3
Phenylphosphoryl dichloride
$POCl_3$, $POBr_3$
$PSCl_3$
$PHal_5$, PCl_5
As_2O_3, As_2O_5
$AsCl_3$
SbF_3, $SbCl_3$, $SbCl_5$
Bi
BiO_3^-
NH_4 vanadate
V_2O_5,Al_2O_3
O_2, O_3
H_2O_2
Peroxide
S
S^{--}, SH^-, SH_2
$(NH_4)_2S_x$
Na formaldehyde sulfoxylate
$S_2O_4^{--}$
Tetrathionate
$SO(NH_2)_2$
Sulfonamide
$SOCl_2$, $SOBr_2$
Sulfonic acid chlorides
Arylsulfonyl chloride
p-Toluenesulfonic acid chloride
SO_2Cl_2
SO_2
$S_2O_5^{--}$
SO_3
$(NH_4)_2SO_3$
$(NH_4)_2SO_4$
Pyridine·SO_3
$HCON(CH_3)_2{\cdot}SO_3$
Sulfonates
Na-m-nitrobenzenesulfonate
$NaHSO_4$, $KHSO_4$, NH_4HSO_4
Ethanesulfonic acid
Benzene-, p-Toluene-, Naphthalene-β-sulfonic acid
HSO_3NH_2
NH_2OSO_3H (Hydroxylamine-O-sulfonic acid)
H_2SO_4
H_2SO_5
$S_2O_3^-$
$(NH_4)_2S_2O_8$

$S_2O_8^{--}$
FSO_3H, $ClSO_3H$
Sulfur chlorides
S_2Cl_2
Se
SeO_2
Chromite
$CuCr_2O_4$, $CuCr_2O_4$-C
$(Ca,Cu)Cr_2O_4$, $(Ba,Cu)Cr_2O_4$
Cr_2O_3,Al_2O_3
MoO_x, MoO_3
CrO_4^-, $Cr_2O_7^{--}$, CrO_3
MoS_2
CrO_2Cl_2
$CrCl_2$
I_3^-
Halogen
Cl, Br, I
BrCN
IF_5, ICl, ClI, BrI
Alkyl hypochlorite
$HalO^-$, ClO^-
NaOCl, KOBr, KOI
$Ca(OCl)_2$, $Ba(OI)_2$
ClO_3^-, BrO_3^-
$KClO_3$, $NaBrO_3$, KIO_3
$HClO_4$
IO_4^-
Cl^-, I^-
NH_4F, NH_4Cl, NH_4I
Hydrochlorides
Pyridine hydrochloride
Acetylpyridinium chloride
Hydrobromides
$(CH_3)_4NBr\cdot Br_2$
Pyridine hydrobromide-perbromide
Acids/metal chlorides
Mineral acids
Hydrogen halides
HF, HCl, HBr, HI
MnO_2
MnO_4^-
$NaMnO_4$, $KMnO_4$, $Ba(MnO_4)_2$
Fe
Fe/Fe^{++}
FeS/Al_2O_3
$FeSO_4$
$Fe_2(SO_4)_3$
$FeCl_3$
Fe^{+++}
$Na_3[Fe(CN)_5NH_3]$
$K_3[Fe(CN)_6]$
Co
Co/Al_2O_3
$Co(CO)_4$
Cr_2O_3-cobalt hydrate-$CaCO_3$
Co nitrite
$CoCl_2$
CoF_3
Ni
Ni-Al
Ni/Pt, $Ni/PtCl_4$
Ni,Cr_2O_3
Nickel-zinc chromite
$Ni(CO)_4$
$NiSO_4$
RuO_2
Pd
Pd-$CaCO_3$, Pd-$SrCO_3$, Pd-$BaCO_3$
Pd-$BaSO_4$
Pd-C
Pd-pumice
PdO
OsO_4
Pt
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PtO_2
v.i.

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